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Accelerometer-Determined Physical Behavior Metrics and their Associations with Sarcopenia among Oldest-Old Adults

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ACCELEROMETER-DETERMINED PHYSICAL BEHAVIOR METRICS AND THEIR ASSOCIATIONS WITH SARCOPENIA AMONG OLDEST-OLD ADULTS

A Thesis Presented

by

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ABSTRACT

ACCELEROMETER-DETERMINED PHYSICAL BEHAVIOR METRICS AND THEIR ASSOCIATIONS WITH SARCOPENIA AMONG OLDEST-OLD ADULTS

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INTRODUCTION: Sarcopenia is a loss of muscle function and muscle mass which frequently occurs among the oldest-old adult population (aged 85+ years). The analysis of accelerometer-determined physical behavior volumes and patterns of oldest-old adults might provide novel insights into the associations with sarcopenia and its components. **METHODS**: A total of 145 participants in the primary sample and 87 participants in the subsample with a mean age of 88.2 (2.5) years from the Health, Aging, and Body Composition study cohort provided cross-sectional data of handgrip strength, appendicular lean mass, gait speed, and accelerometry. Probable, confirmed, and severe sarcopenia were assessed based on the revised definition of the European Working Group on Sarcopenia in Older People 2. Binomial logistic and multivariate linear regression models as well as dose-response analyses were applied and adjusted for demographics, accelerometer wear time, lifestyle factors, and chronic health conditions. **RESULTS:** Oldest-old adults with higher total volumes of moderate to vigorous physical activity (MVPA) (OR=0.74, 95% CI 0.62 to 0.89) showed a lower likelihood for a probable sarcopenic condition in the primary sample. Likewise, patterns of higher accumulated

time spent in MVPA bouts of less than 10 minutes (OR=0.78, 95% CI 0.64 to 0.95) and MVPA bouts of at least 10 minutes (OR=0.78, 95% CI 0.63 to 0.98) were also related with lower odds of probable sarcopenia. A 2.1 times (95% CI 1.01 to 4.35) higher likelihood for confirmed sarcopenia was observed among participants who spent 60 minutes more per day in sedentary behavior (SB). Furthermore, 2.9 times (95% CI 1.05 to 8.02) greater odds of severe sarcopenia were identified following each 0.1 higher active-to-sedentary transition probability (ASTP). Focusing on individual sarcopenic components, higher total activity counts, higher MVPA, higher light intensity physical activity (LIPA), lower SB, and lower ASTP were related with better gait speed.

CONCLUSION: The total volume of MVPA, whether accumulated in short sporadic bouts or prolonged bouts, was associated with lower odds of probable sarcopenia. Higher LIPA, lower SB, and a less fragmented activity pattern might also be related with a lower likelihood of sarcopenia status and better physical performance among oldest-old adults.

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LIST OF ABBREVIATIONS

ASTP – Active-to-sedentary transition probability

AWGS – Asian Working Group for Sarcopenia

BIA – Bioelectrical impedance analysis

BMI – Body mass index

CI – Confidence Interval

cpm – Counts per minute

DXA – Dual-energy X-ray absorptiometry

EWGSOP – European Working Group on Sarcopenia in Older People

EWGSOP2 –European Working Group on Sarcopenia in Older People 2

FNIH – Foundation for the National Institutes of Health

Health ABC – Health, Aging, and Body Composition

IPAQ – International Physical Activity Questionnaire

LIPA – Light intensity physical activity

MVPA – Moderate to vigorous physical activity

METs – Metabolic equivalents

OR – Odds ratio

PA – Physical activity

PAG – Physical Activity Guidelines for Americans

SB – Sedentary behavior

ß – Beta coefficient

CHAPTER 1

INTRODUCTION

1.1 Background

Steady age-related decreases in muscle strength, muscle mass, and various physical performance measures occur simultaneously.[1] This progressive and generalized loss of muscle function and mass is recognized as sarcopenia which is associated with diminished functional ability, poor quality of life, greater fall-related injuries, more frailty, and increased all-cause mortality among older adults.[2–4] Sarcopenia affects more than 50 million people today and will impair more than 200 million people in the upcoming 40 years.[5] In 2014, the global economic burden was estimated at USD $40.4 billion from this skeletal muscle disorder.[6]

The prevalence of sarcopenia and the related economic burden are expected to rise substantially in the foreseeable future due to the rapid global increase in the number of people aged 65 and older.[1] In this context, the oldest-old adult population (aged 80-85 years and older) demonstrate the highest growth rate which is anticipated to expand threefold between 2015 and 2050.[7] This increasing proportion of older individuals can be explained by improved living conditions and advancing medical care.[3]

The modifiable characteristics of physical behavior may include huge opportunities to reduce the prevalence of sarcopenia in the community. Consequently, the purpose of this thesis is to evaluate the associations of various physical behavior metrics with sarcopenia and its components among oldest-old adults.

1.2 Past and Present Definition of Sarcopenia

The term sarcopenia was coined by Rosenberg in 1988 by combining the Greek words “sarx” which means “flesh” and “penia” which means “deficiency” to describe the paucity of muscle tissue often observed in older adults.[8] Based on this definition, Baumgartner et al.[9] developed the first epidemiological approach in 1998 to estimate the prevalence of sarcopenia by the application of an anthropometric equation in which the appendicular skeletal muscle mass was computed and evaluated. Soon after, researchers ascertained that muscle quantity alone was not pivotal as a parameter of adverse events and poor health outcomes.[10] In 2010, the initial sarcopenia definition on the basis of low muscle mass was extended by adding muscle strength and physical performance.[10] This move imposed by the European Working Group on Sarcopenia in Older People (EWGSOP) in 2010 was supported within the field of geriatrics.[11] Just 28 years after its first terminological appearance, sarcopenia was formally recognized as a muscle disease by the World Health Organization in 2016 with its own International Classification of Disease, Tenth Revision, Clinical Modification code.[12]

Between then and now, the interest on sarcopenia has exponentially grown in the scientific community.[8] Classifying this geriatric condition as a disease has allowed physicians to run diagnostics and researchers to investigate an officially accepted health outcome.[13] After defining sarcopenia by measures of muscle strength, muscle mass, and physical performance in 2010,[10] several other definitions, namely the International Working Group on Sarcopenia in 2011,[14] the Asian Working Group for Sarcopenia (AWGS) in 2014 and its updated version in 2019,[15,16] the Foundation for the National Institutes of Health (FNIH) in 2014,[17] and the revised definition of the European Working

Group on Sarcopenia in Older People 2 (EWGSOP2) in 2019,[18] were developed with differences in their methodological approach.[19] These operational dissimilarities are also based on racial and ethnic differences in body composition and grip strength.[20] As a consequence, epidemiological prevalence studies vary substantially and depend on the definition used.[20] For instance, lower estimates of sarcopenia are usually stated in studies which included measures of muscle function or physical performance in addition to muscle mass.[21] Likewise, differences in participant age, applied muscle mass cut points, and the utilization of dual-energy X-ray absorptiometry (DXA) versus bioelectrical impedance analysis (BIA) may cause substantial study outcome deviations.[21] This highly diverse application of definitions results in diagnosis rates of 1-29% in community-dwelling populations and of 14-33% among residents living in long-term care facilities.[19] Another systematic review and meta-analysis found that the prevalence of sarcopenia was between 24-40% for single measure definitions and 10-19% by employing combined definitions.[21]

At this point, the most used and cited definition is the one presented by the EWGSOP.[10] Members of the EWGSOP revised their definition of sarcopenia and created the EWGSOP2 a few years later.[18] Disparities between the EWGSOP and the modified EWGSOP2 are obvious due to alterations of cut-off values for determining low muscle strength and low muscle mass measures.[22] These changes have shown substantial deviations in the prevalence rate of investigated populations.[22] Nevertheless, EWGSOP2 is the only definition endorsed and supported by a range of international scientific societies such as the AWGS, the European Geriatric Medicine Society, the European Society for Clinical Nutrition and Metabolism, the European Society for Clinical and

Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases, International Osteoporosis Foundation, and International Association of Gerontology and Geriatrics European Region for research and clinical practice.[18]

Table 1: EWGSOP2 sarcopenia cut-off values applied in our analyses

Test	Measurement tool	Cut-off points for men	Cut-off points for women
EWGSOP2 sarcopenia cut-off points for low muscle strength			
Grip strength	Isometric handheld dynamometer	**<27 kg**	**<16 kg**
EWGSOP2 sarcopenia cut-off points for low muscle mass			
Appendicular lean mass	DXA	**<20 kg**	**<15 kg**
EWGSOP2 sarcopenia cut-off points for low physical performance			
Gait speed	20-meter course	**≤0.8 m/s**	

The definition of EWGSOP2, which will be applied in our study, identifies probable, confirmed, or severe sarcopenia. In this regard, the detection of low muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women) predicts a probable sarcopenia diagnosis.[18] This diagnosis can be confirmed after the observation of low muscle mass by using body composition measures (i.e., appendicular lean mass: <20 kg for men and <15 kg for women).[18] Furthermore, low physical performance measures, which can be assessed by a variety of tests (i.e., gait speed: ≤0.8 m/s), provide information on the severity of sarcopenia.[18] A severe sarcopenia diagnosis will be determined when all three sarcopenia-relevant indicators, including muscle strength, muscle mass, and physical performance, show measures below the specified cut-off points.[18] All sarcopenic parameters and their cut-off values are illustrated in Table 1.

1.3 Muscle Strength and Muscle Mass Change across the Lifespan

A considerable amount of evidence regarding the variation of muscle strength and muscle mass across a lifetime in the current literature is available, showing both variables start to decline at about the fourth decade with heterogenous changes in time and magnitude.[23]

Muscle Strength: As illustrated by Dodds et al.[24], normative data from twelve British studies of grip strength across the life course suggests that grip strength increases in youth and young adulthood with a peak reached in early adulthood (up to ~40 years of age).[24] Strength in men and women may develop at a similar pace until adolescence.[24] This phase is followed by a more pronounced and rapid strength gain to a higher peak median in males compared to their female counterparts.[24] The muscle strength then steadily declines from midlife onwards in both sexes with an annual decrease of 1.5% and an even more accelerated reduction of around 3% per year after the age of 60.[24,25] By age 80, the prevalence of weak grip strength is approximately 23% in males and 27% in females.[24]

Muscle Mass: Similarly, the decline in skeletal muscle mass starts dwindling in the third or fourth decade of life.[19] Researchers estimate that approximately 20% of muscle mass can be lost by the age of 70 years.[26] While men usually show higher muscle mass accumulations over time, they also suffer greater losses of muscle mass in later adulthood and old age.[25] Overall, after the age of 35 years, healthy men and women can expect a loss in muscle mass of around 1-2% per year.[27]

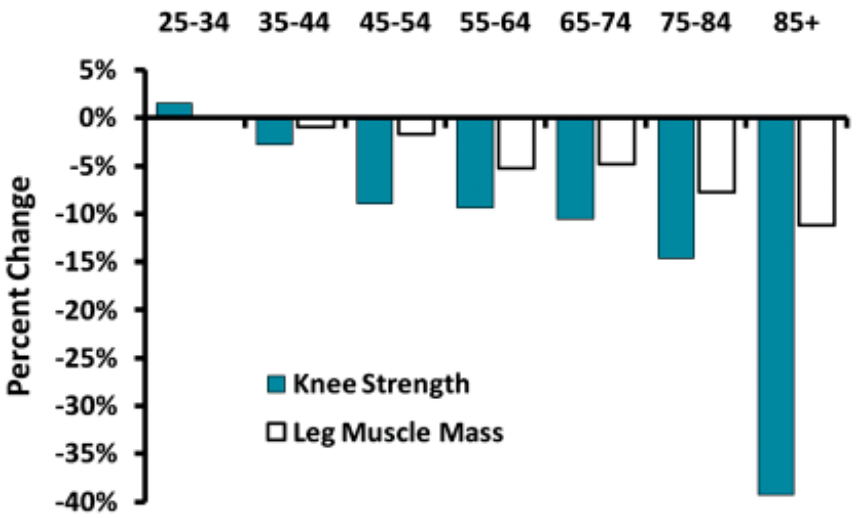

Figure 1: Disproportionate decline of leg muscle strength and leg muscle mass across the life course. Figure adopted from Ferrucci et al.[23].

With advancing age, there is an obvious tendency of disassociation between changes in muscle strength and muscle mass (Figure 1).[23] Findings of a longitudinal study indicate that even well-functioning older men and women revealed a 3-fold greater loss in muscle strength than in muscle mass over the course of 3 years of follow-up.[28] Several other studies have already confirmed the hypothesis that the decrease in muscle strength is much greater than the decline in muscle mass.[2,23,24,29] As a consequence, muscle strength has been considered as the key characteristic to diagnose sarcopenia.[18]

Muscle power, which is specified as the product of force and velocity of muscle contraction, has shown an earlier and more drastic decline with aging compared to muscle strength and muscle mass.[29,30] In this context, muscle power has been identified as a better predictor of functional performance measures than other sarcopenic parameters among older adults.[30] However, the demand of clinical settings with expensive tools, the necessity of a time-consuming training for clinicians and subjects, and the lack of standardized protocols to define low muscle power were stated as the

main barriers to consider this metric as an assessment instrument in sarcopenia research.[31] Consequently, muscle power has been largely disregarded in previous muscle health-related investigations.[31] There is a growing interest in the field of geriatrics to create valid muscle power measurements with better applicability in research,[32,33] which would provide the opportunity for a standardized protocol with more reliable cut-off points to diagnose sarcopenia.

1.4 Contributing Causes of Sarcopenia and the Relevance of Physical Behavior

According to the definition imposed by EWGSOP2, the combination of low muscle strength and mass is used to diagnose sarcopenia in clinical practice.[18] This state of skeletal muscle failure or insufficiency may occur due to a chronic degradation of muscle strength and muscle mass with time or with sudden disease/immobility.[2] Skeletal muscle deterioration with aging is attributed to a combination of primary and secondary factors.[2] Primary sarcopenia is specified as a progressive loss of muscle quantity and quality with advancing age when no other cause is evident.[2] In this context, age-related dysfunctions of the mitochondria, the satellite cells, and the neuromuscular system are associated with primary sarcopenia.[34] Steady decreases in hormone concentrations such as growth hormone, testosterone, thyroid hormone and insulin-like growth factor may also contribute to the reduction of muscle mass and strength during aging.[35] Higher levels of pro-inflammatory cytokines, including tumor necrosis factor alpha and interleukin-6, produce catabolic signals which can diminish muscle conditions.[35] Secondary aging, on the other hand, is influenced by lifestyle factors, environmental influences, or diseases.[36] Nutritional-, inactivity-, disease-, and iatrogenic-related health issues are stated as the most frequent underlying causes of secondary sarcopenia.[2] The differentiation between

primary and secondary sarcopenia is crucial due to therapy planning.[5] By knowing and detecting the course of these two sarcopenic manifestations, early treatment of underlying secondary sarcopenia can prevent additional wasting of muscle quality and quantity which further helps to avoid other health complications.[5]

Soon after reaching the peak of muscle mass in early adulthood, the primary age-related loss of muscle mass indicates a continuous linear decline.[37] On the contrary, muscle wasting originated from secondary sarcopenia causes a non-linear decline with greater progressive decreases.[37] For instance, as part of a cachexic syndrome, cancers of advanced stage can lead to an exponential muscle loss of up to 15% per 100 days which is equivalent to approximately 30 years of aging.[37] Even more pronounced are the changes of muscle strength and mass produced by limb immobilization.[38] In this regard, the disuse of leg muscles for the duration of 4 to 7 days can lead to a 2-6% reduction of muscle mass and an 8-22% decrease of muscle strength in young as well as older adults.[38] Malnutrition is also stated as an essential underlying culprit for the development of sarcopenia. Older adults commonly show a diminished intake of vital proteins which are essential for a well-functioning muscle metabolism.[25] This protein-energy malnutrition negatively affects muscle functions.[25] Study results of a four-year follow-up study suggest an almost four times higher risk of acquiring sarcopenia during a malnutritional state.[39]

Low physical activity (PA) levels are also stated as a main contributor for the development of sarcopenia.[13,40,41] Reductions in the overall number of steps per day (from 6,000 – 10,000 steps per day to less than 1,000 – 1,500 steps per day) can promote a progressive depletion of muscle strength and mass.[42,43] High volumes of sedentary

behavior (SB), on the other hand, might accelerate the loss of muscle quality and quantity among older adults.[44] Previous research has demonstrated that self-reported prolonged sitting time is associated with higher odds of sarcopenia in older adults regardless of the total time spent in higher PA intensity categories.[45] This underscores the independent influence of PA and SB on sarcopenia and its parameters.[44] Overall, being physically active across the life course has shown strong associations with better musculoskeletal health (Figure 2).[7]

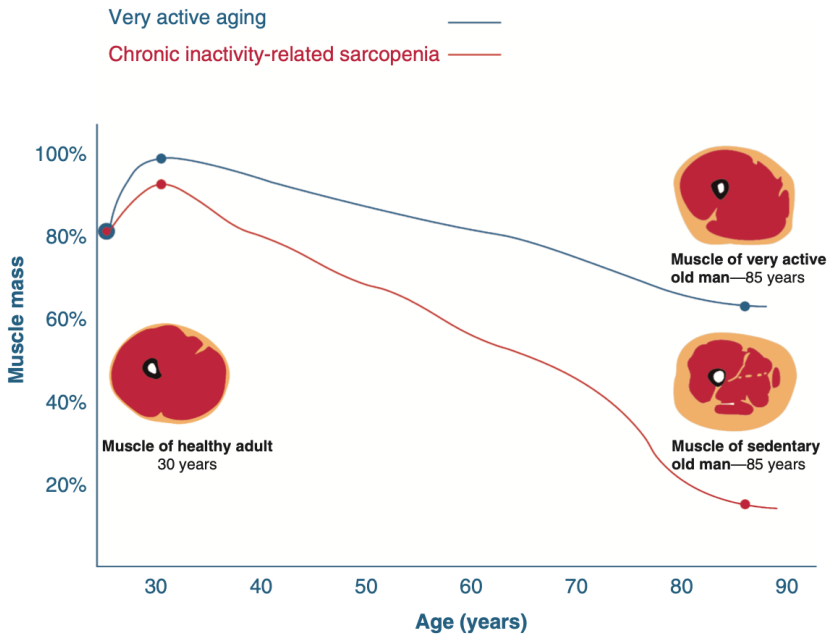

Figure 2: Muscle mass changes across the life course among a very active and a sedentary old man. Figure adopted from Valenzuela et al.[7].

Prior analyses have indicated that few older adults produce PA bouts longer than 10 minutes.[46,47] In this context, PA patterns change considerably with aging by displaying more fragmented daily patterns with shorter active bouts and longer sitting periods (Figure 3).[48–50] These activity patterns can look very different and depend on the functional status of each individual.[48] For instance, while a healthy older adult may

accumulate activity minutes in one single bout, individuals with functional limitations might not be able to sustain activity bouts for a long period of time which results in a more frequent compensatory interchange between PA and SB during a day.[48] Research has shown that fragmented daily patterns are associated with worse physical performance measures,[48] higher fatigability,[50] cognitive impairment,[51] and a greater mortality rate among older adults.[49] As a consequence, transition states between sedentary and active behavior may become more important with advancing age.[48–51]

Figure 3: Physical activity pattern change with aging. Figure provided by Jennifer A. Schrack, PhD.

1.5 Statement of the Problem

The progressively increasing demographic growth of older adults globally leads to major challenges for public health and medicine to prevent and combat age-related diseases such as sarcopenia.[7] Due to the absence of effective drugs, PA seems to be the most promising factor to manage sarcopenia.[7] Incorporating various aerobic and strengthening exercises have shown to provide beneficial effects on the functional ability in the oldest-old adult population.[7] Especially PA, with a focus on resistance exercises, is recommended in the prevention and management of sarcopenia according to the

International Clinical Practice Guidelines for Sarcopenia.[13] While progressive resistance training may enhance muscle strength and physical performance, muscle mass seems to be less affected by this intervention.[52] The improvements in muscle strength and physical performance may refine activities of daily living such as walking endurance, gait speed, and stair climbing.[53] However, fewer than 10% of older adults achieve the recommended amount of two strength trainings per week.[54,55] Besides reported issues at the training facilities such as unavailability of type-, age-, and time-specific classes or poor staff support, worse health conditions caused by injury and illness are stated as the most common reasons among older adults to avoid participating in resistance training.[56]

Researchers and clinicians may also consider interventions which are more easily adopted by older adults.[53] The principle that any activity is better than no activity might also apply for the prevention of sarcopenia. Consequently, feasible and pragmatic daily PA tasks for vulnerable older adults should receive more attention in the field of geriatrics. Gaining a better understanding of daily PA behavior and its association with sarcopenia is of utmost importance to create novel and efficient interventions.

Detailed PA patterns consisting of bouts with various frequencies, intensities, and durations can be captured by contemporary research-based accelerometers.[49,57] Within this framework, the total volume of PA is specified as an amalgamated metric which summarizes all performed PA bouts.[58] The 2nd edition of the Physical Activity Guidelines for Americans (PAG) released by the U.S. Department of Health and Human Services in 2018 suggests that people aged 65 and above should engage in a minimum of 150 minutes of moderate to vigorous intensity physical activity (MVPA).[59] Recommended PA bouts of at least 10 minutes which were stated in previous versions of

PA recommendations, including the PAG 2008 and the global recommendation on PA for health 2010,[60,61] were removed from the recently revised PAG 2018.[59] This paradigm shift occurred based on the growing evidence that PA of any bout duration is associated with better health outcomes.[62] However, the efficacy of the accumulated time spent in short PA bouts (<10 minutes) as well as long PA bouts (≥10 minutes) compared to the overall volume of PA is still unknown,[63] especially in association with detrimental health outcomes such as sarcopenia.[64,65]

To the best of our knowledge, only one study has yet investigated associations of objectively measured PA patterns compared to the overall volume of PA on defined sarcopenia and its indicators.[66] Nevertheless, not a single study has included short PA bouts (<10 minutes) to this examination. The assessment of the differentiation between PA patterns and the total sum of PA in various intensities is highly relevant for the development of future health guidelines to prevent sarcopenia in the oldest-old adult population.

1.6 Study Approach

The overall goal of this study is to investigate the associations of accelerometer-measured PA patterns and the total volume of PA with EWGSOP2 defined sarcopenia and its components, including muscle strength, muscle mass, and physical performance, among oldest-old adults. We will also complete dose-response associations of different patterns, volumes, and intensities of PA with sarcopenic conditions and their specified sarcopenia-related markers. These analyses will be realized with cross-sectional cohort data provided by the Health, Aging, and Body Composition (Health ABC) study which offers a comprehensive data collection with measurements on muscle strength, muscle

mass, physical performance, and accelerometry.[67] A sample of 145 oldest-old adults with a mean age of 88.2 (2.5) years from the metropolitan areas of Memphis, TN and Pittsburgh, PA helps address our research aims. We hypothesize that PA patterns comprised of high levels of short MVPA bouts (<10 minutes) are equally important as the total volume of MVPA with EWGSOP2 defined sarcopenia and its parameters among oldest-old adults.

This study will contribute valuable knowledge to the current literature. Addressing this research question will provide information on PA duration and intensity that can be applied in PA interventions to delay or even prevent the loss in muscle strength, muscle mass, and physical performance abilities and thus the onset of sarcopenic conditions among the oldest-old adult population. In the long term, understanding optimal patterns of PA for pragmatic targets for future interventions and public health guidelines focusing on sarcopenia and its components can improve the quality of life and longevity in oldest-old adults.

1.7 Aims and Hypotheses

Aim 1: Examine associations of accelerometer-determined physical behavior volume and pattern metrics with EWGSOP2 defined sarcopenia and its components, including muscle strength, muscle mass, and physical performance, among oldest-old adults. We hypothesize that higher volumes of MVPA, regardless of its accumulation in short MVPA bouts (<10 minutes) or in long MVPA bouts (≥10 minutes), will demonstrate associations with lower odds of EWGSOP2 defined sarcopenia and better sarcopenic parameters among oldest-old adults.

Aim 2: Examine dose-response associations of various accelerometer-determined physical behavior volume and pattern metrics with EWGSOP2 defined sarcopenia and its components, including muscle strength, muscle mass, and physical performance, among oldest-old adults. Physical behavior metrics will be grouped into tertiles. This enables us to determine health-beneficial doses for different patterns, volumes, and intensities of physical behavior on EWGSOP2 defined sarcopenia and its determinants among oldest-old adults. We hypothesize that oldest-old adults with the highest volumes of MVPA, whether accumulated in short MVPA bouts (<10 minutes) or in long MVPA bouts (≥10 minutes), will indicate favorable dose-response associations with EWGSOP2 defined sarcopenia and its individual parameters.

CHAPTER 2

LITERATURE REVIEW

Since the coining of the term sarcopenia by Rosenberg in 1988[8] and the official recognition as a muscle disease in 2016 by the World Health Organization,[12] a gradual increase of scientific interest and awareness about this public health issue has occurred. The purpose of this literature review is to summarize and discuss crucial findings regarding the association of various physical behavior metrics with defined sarcopenia and its related parameters, including muscle strength, muscle mass, and physical performance, in older adults.

2.1 Methodological Approach for the Literature Review

This literature search was completed by using the Covidence software which is a literature review manager software and a useful tool to screen research articles and summarize information from the existing literature. The literature review was conducted by implementing the following steps: (1) topic-specific literature search in an electronic database, (2) importing selected literature to Covidence, and (3) including or excluding relevant literature based on abstract- as well as full-text screening within the software. Research articles were collected from PubMed using the following Boolean string: "sarcopenia AND (physical activity OR sedentary behavior) AND (questionnaire OR self-report OR acceleromet* OR objectively-measur*)". This procedure identified 391 articles. After additionally screening the reference lists of individual research articles, 9 supplemental studies were included in Covidence. As a result, 400 scientific papers were evaluated in the initial screening.

Research articles were included based on the following criteria: 1) observational studies; 2) community-dwelling population; 3) age 60 and above; 4) measurement of physical activity by using self-report and/or accelerometer; 5) measurement of muscle strength; 6) data for associations of PA with sarcopenic determinants including muscle strength, muscle mass, or physical performance and/or defined sarcopenia. Excluded were research articles with the following attributes: 1) review articles and meta-analyses; 2) randomized controlled trials; 3) measurements of muscle mass and/or physical performance alone; 4) accelerometer-assessed data without any information on at least one of the following physical behavior metrics: total volume of PA, light intensity physical activity (LIPA), moderate to vigorous physical activity (MVPA), bouts of PA, total time spent in SB or bouts and breaks in sedentary time. Due to the limited data among the oldest-old adult population, we decided to collect studies with all older adults defined at 60+ years of age. In this abstract screening process, a total of 265 studies were considered as irrelevant and thus excluded from this literature review. The remaining 135 studies were assessed for eligibility by reviewing the full text of the study. This full text review led to an additional exclusion of 111 studies since they provided outcomes, study designs, populations or settings which did not match the determined inclusion criteria. Overall, 24 research articles met the inclusion criteria and were selected for a comprehensive literature review (Figure 1).

Figure 4: Literature review summary table from Covidence regarding the associations of physical behavior metrics with defined sarcopenia and/or its components.

2.2 Association of Physical Activity with Defined Sarcopenia and its Components among Older Adults

2.2.1 Self-report Measurement of Physical Activity

Overview: 16 out of 24 studies used self-report questionnaires for the assessment of PA. This high proportion of employing subjective methods was expected since measuring PA by questionnaire is known to be more cost-effective and simpler to administer in comparison to accelerometry.[68] High costs and a lack of technical expertise are stated as the most common barriers for applying accelerometers in epidemiological research.[69] Self-report measurements are still considered as a solid method for studies with large populations.[69] In addition, questionnaires provide the ability to evaluate different types of PA and can be applied for a long period of time.[70]

Since PA is a multidimensional construct, each instrument has its strengths and limitations which explains the absence of a gold-standard subjective method.[71] The

International Physical Activity Questionnaire (IPAQ) is still the most used self-report PA questionnaire globally.[72] This also remains true for our literature review in which one quarter of the studies conducted the IPAQ.

Study Outcomes Review: As illustrated in Table 2, the association of self-report PA with defined sarcopenia and its components, including muscle strength, muscle mass, and physical performance, provided conflicting information. These inconsistent results may be caused by the diversity of applied self-report methods to evaluate PA and the various approaches to define sarcopenia. Notably, the measurement of gait speed as an indicator of physical performance was most frequently related with self-report PA.

Several unique findings from the self-report PA studies were of interest. Structured daily schedules with frequent engagement in active hobbies across the life course may help to maintain better muscle health among the old-age population.[73] The transition from work life to retirement might be a vital point in time due to critical alterations on the structure of daily routines.[73] Outcomes from a Japanese population-based cohort study indicated a significant relationship between exercise habits in middle age and sarcopenia in older age even after adjusting for age, sex, and body mass index.[74] Older adults with higher PA levels were more likely to remain in the normal muscle health state which was described as having muscle strength, muscle mass, and physical performance above the specified cut-off values for sarcopenia.[75] However, according to longitudinal outcomes from Yu et al.[76], once participants were diagnosed with sarcopenia, the number of returns to a non-sarcopenic condition was low. Based on this information, higher levels of PA may prevent older adults of becoming sarcopenic but may not be effective enough to help achieve a return to a non-sarcopenic state.

Table 2: Characteristics of observational studies looking at associations of self-report physical activity with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Akune et al. (2014)[74]	Cross-sectional	65+	1000	Japan	Interviewer-administered questionnaire	EWGSOP	Grip strength	BIA	Gait speed; RCS; One-leg standing time	While current walking habits indicated no association with sarcopenia, individuals with exercise habits in middle age had significantly lower odds for sarcopenia.
Alexandre et al. (2014)[77]	Cross-sectional	60+	1149	Brazil	Brazilian version of the IPAQ	EWGSOP	Grip strength	DXA	Gait speed	Other than men, women with low levels of PA were associated with a lower likelihood for sarcopenia.
Bann et al. (2015)[78]	Cross-sectional	70-89	1130	USA	CHAMPS	N/A	Grip strength	N/A	N/A	Lower-light, higher-light, and total PA demonstrated no association with MS.
Dutra et al. (2015)[79]	Cross-sectional	60+	173	Brazil	IPAQ, long form	EWGSOP	Grip strength	Lee equation	Gait speed	Participants (≥ 80 years) with insufficient PA levels had higher odds for a sarcopenic condition.

Gianoudis et al. (2015)[45]	Cross-sectional	60-86	162	Australia	CHAMPS	EWGSOP	Knee extensor strength	DXA	RCS; Four square step test; TUG	Higher levels of MVPA suggested no associations with MS, MM, and PP.
Hai et al. (2017)[80]	Cross-sectional	60-92	836	China	IPAQ, long form	AWGS	Grip strength	BIA	Gait speed	The association between PA levels and sarcopenia was not significant in the multivariate analysis.
Hai et al. (2017)[81]	Cross-sectional	60-92	834	China	IPAQ, long form	AWGS	Grip strength	BIA	Gait speed	The multivariate model demonstrated no link between PA and sarcopenia.
Kim et al. (2019)[82]	Cross-sectional	65+	3634	South Korea	N/A	N/A	Grip strength	N/A	N/A	Higher participation rates in aerobic and strengthening exercise were significantly associated with better MS in men and women.
Mijnarends et al. (2016)[83]	Cross-sectional and Cohort	66-93	2309	Iceland	N/A	EWGSOP	Grip strength	CT	Gait speed	More than 1 hour per week of MVPA was correlated with lower odds of sarcopenia.
Murphy et al. (2014)[75]	Cross-sectional and Cohort	70-79	2928	USA	Standardized questionnaire designed specifically for the Health ABC study	N/A	Grip strength	DXA	Gait speed	Higher levels of PA lowered the likelihood of transitioning toward a sarcopenic state.

Sjöblom et al. (2020)[84]	Cross-sectional and Cohort	66-71	610	Finland	Self-administered questionnaire	N/A	Grip strength	DXA	RCS; ability to squat; gait speed; tandem walk; standing with closed eyes; modified SPPB; one leg stance performance	Several PP measures were positively linked with continuous PA at 1-hour intervals. Higher continuous PA at 1-hour interval with a total volume of PA ≥ 2.5 hours per week was correlated with better walking speed and ability to squat.
Volpato et al. (2014)[85]	Cross-sectional	65+	538	Italy	Self-administered questionnaire	EWGSOP	Grip strength	BIA	Gait speed	Low levels of PA were not related with sarcopenia.
Xu et al. (2018)[86]	Cross-sectional	60+	2633	China	Validated questionnaires used in the China Kadoorie Biobank study	AWGS	Grip strength	BIA	Gait speed; RCS; TUG	Higher levels of PA were significantly correlated with better grip strength and better gait speed measures.
Yang et al. (2017)[87]	Cross-sectional	65+	844	Taiwan	N/A	N/A	Grip strength	DXA	Gait speed	Lower MS, MM, and PP measures were related with the joint association of physical inactivity and poor insulin sensitivity.

Yu et al. (2014)[76]	Cohort	65+	4000	China	PASE	EWGSOP	Grip strength	DXA	Gait speed	The risk of sarcopenia was lower in participants with higher total volumes of PA. Higher levels of PA were not correlated with the reversibility of a lower risk for sarcopenia.
Zeng et al. (2016)[73]	Cross-sectional	60+	461	China	N/A	AWGS	Grip strength	BIA	Gait speed; RCS	Only gait speed as a metric of PP was positively associated with physical exercise.

Abbreviations: AWGS: Asian Working Group of Sarcopenia; BIA: bioelectrical impedance analysis; CHAMPS: Community Healthy Activities Model Program for Seniors; CT: computerized tomography; DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; IPAQ: International Physical Activity Questionnaire; MM: muscle mass; MS: muscle strength; MVPA: moderate to vigorous physical activity; N/A: Not available; PA: physical activity; PASE: Physical Activity Scale for the Elderly; PP: physical performance; RCS: repeated chair stand test; SPPB: short physical performance battery; TUG: timed up and go test.

2.2.2 Objective Measurement of Physical Activity

Overview: A total of 9 investigations applied objective measurements to examine associations of behavioral activity with defined sarcopenia and its parameters. Accelerometers used in PA research are small wearable devices with the main purpose of recording accelerations triggered by body movements. This allows the collection of various PA-related measures in a free-living environment.[70] Accelerometry has gained popularity among researchers in recent decades since its usage solved several limitations of subjective assessments such as lack of robustness to estimate light or moderate intense activities or to quantify energy expenditure.[71] The issue of recall bias can be reduced with accelerometers which alleviates the risk of human error.[88] The unique capability of accelerometry to translate objectively measured acceleration counts via designed algorithms into PA intensity, volume, and duration, or metrics such as energy expenditure is another advantage over self-report methods.[71,88]

The ActiGraph (Pensacola, FL, USA) has been the most used accelerometer by researchers with a utilization rate of more than 50% among published studies according to a systematic review.[89] Based on our literature search, more than half of the collected studies (5 out of 9 articles) employed ActiGraphs to assess different activity behavior variables in older adults.

Provided data and information from these scientific articles are summarized in detail below with a focus on observational findings of the association of various physical behavior metrics, including the total volume of PA, LIPA, MVPA, and bouts of PA, with defined sarcopenia as well as sarcopenia-relevant indicators including muscle strength, muscle mass, and physical performance.

2.2.2.1 Total Volume of Physical Activity

Overview: The total volume of PA is a summarizing metric which includes the dimensions of frequency, intensity, and duration of activity bouts.[58] Accelerometry has the ability to provide total activity counts which indicates an estimation of the total time spent in PA.[58]

Study Outcomes Review: 4 out of 9 studies from our literature review investigated the association of the accelerometer-assessed total volume of PA with defined sarcopenia and its determinants (Table 3). Higher total activity counts were significantly related with lower odds of sarcopenia.[64,90] In this context, Sanchez-Sanchez et al.[64] demonstrated a positive correlation between total activity counts and all sarcopenia-relevant indicators including muscle strength, muscle mass, and physical performance. Westbury et al.[90] also reported associations of higher accelerometer-assessed volumes of PA with a lower likelihood of sarcopenia and better gait speed as a measure of physical performance. However, converse to the previous findings from Sanchez-Sanchez et al.[64], there were no significant correlations with muscle strength and muscle mass. In addition, Bann et al.[78] reported a link between objectively measured PA and grip strength in men, but not in women. This gender-specific difference may be explained by the types of upper limb strengthening activities in which men may partake more frequently than women.[78] While overall levels of PA were inconsistently related with muscle strength and muscle mass measures, physical performance indicated a significant association with the total quantity of activity across all collected studies.

Table 3: Characteristics of observational studies looking at associations of total activity counts with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Bann et al. (2015)[78]	Cross-sectional	70-89	1130	USA	ActiGraph GT3X: Total PA (min/day)	N/A	Grip strength	N/A	N/A	Higher levels of PA were significantly associated with better grip strength in men but not in women.
Rojer et al. (2018)[91]	Cross-sectional	74.4 (72.4 - 78.0)	80	Netherlands	DynaPort MoveMonitor: Active duration (min/day); Mean duration of active period (second/period)	N/A	Grip strength	BIA	Gait speed	Gait speed as a measure of PP was positively correlated with the overall volume of PA.
Sánchez-Sánchez et al. (2019)[64]	Cross-sectional	78.08 (5.71)	512	Spain	ActiGraph: TAC per day	FNIH	Grip strength	DXA	Gait speed	Defined sarcopenia and its components, including MS, MM, and PP measures, were positively related with TAC.
Westbury et al. (2018)[90]	Cross-sectional	74-84	131	UK	GENEactiv: Daily time spent in non-sedentary PA levels (≥40 acceleration in milli-g)	EWGSOP	Grip strength	DXA	Gait speed	Higher levels of PA were linked with better PP and a lower likelihood for a sarcopenic condition.

Abbreviations: BIA: bioelectrical impedance analysis; DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; FNIH: Foundation for the National Institutes of Health; MM: muscle mass; MS: muscle strength; N/A: Not available; PA: physical activity; PP: physical performance; TAC: total activity counts.

2.2.2.2 Light Intensity Physical Activity

Overview: Metabolic equivalents (METs) can estimate the energy expenditure of individuals during PA and is often used as an indicator of activity intensity.[92] In this regard, 1 MET signifies the energy expenditure when sitting or lying at rest and increases during activities in higher intensities.[92] The operational definitions of METs for each activity level are described in Figure 5.[93] Light intensity physical activity (LIPA) is defined by METs of 1.5-2.9 which includes activities such as walking slowly or washing dishes.[94] Health effects of LIPA are poorly understood since most published epidemiological studies use self-report methods which are less successful in capturing lower intensity activities.[94] A meta-analysis from Ku et al.[95] indicated that increased levels of LIPA provide additional health benefits above and beyond levels of MVPA. Due to commonly detected limited physical conditions in older adults, LIPA may offer an effective and feasible opportunity to replace SB which may avoid the onset of related chronic conditions. Since LIPA appears to be less fatiguing, activities in lower intensity categories can be integrated into the entire day with higher frequency and comfort for older adults.

MET categories	≤1.0 to ≤1.5	<1.5 to <3.0	≤3.0 to <6	≤6
Physical activity categories	Sedentary+standing	Light-intensity physical activity	Moderate-intensity physical activity	Vigorous physical activity
Examples of physical activities	Lying, sitting and stationary standing Sitting quietly (eg, watching television and car driving) and standing (eg, during computer work)	Slow walking (<4 km/h) Sitting tasks with moderate effort (eg, operating heavy machinery) and standing with minor effort (eg, active workstation)	Moderate and fast walking (4–7 km/h) Bicycling or walking for transportation and most manual labour (eg, garbage collecting, carpentry, bricklaying or masonry)	Very fast walking (>7 km/h) Running, swimming, bicycling for exercise, carrying heavy loads or moderate loads up a flight of stairs

Figure 5: Operational definitions of metabolic equivalents for each activity category. Figure adopted from Holtermann & Stamatakis.[93]

Study Outcomes Review: In total, 4 investigative papers from our literature search collected LIPA data to analyze its relationship with defined sarcopenia and sarcopenia-relevant metrics (Table 4). The overall tendency of the study outcomes indicated that higher volumes of LIPA were not associated with lower odds of sarcopenia among older adults. While the provided data of the association between LIPA levels and all sarcopenic determinants were inconsistent, physical performance measures seem to be the most influenced parameter. In this regard, Scott et al.[66] reported that an additional hour per week in LIPA led to a 12% higher likelihood of better timed up and go test performance in older adults.

The effect of reducing SB while increasing LIPA tended to diminish the risk of becoming sarcopenic but lacked statistical significance.[64] Significantly lower odds for sarcopenia appeared after reducing the time spent in LIPA while increasing the time spent in MVPA among older adults.[64] Furthermore, a subdivision of LIPA into two intensity categories defined as lower-LIPA and higher-LIPA may provide supplemental information. For instance, Bann et al.[78] characterized low-LIPA as minute-by-minute

acceleration counts between 100 and 1040 while higher-LIPA was identified after reaching between 1041 and 1951 acceleration counts per minute. In this context, an additional hour of higher-LIPA led to a 6 kg or a 19% higher performance in grip strength among men.[78] In summary, these study results may conclude just minor effects of LIPA on muscle strength and muscle mass but a positive association with physical performance. As a consequence, spending more time in LIPA might not influence muscle strength and muscle mass but may be important for maintaining physical performance.

Table 4: Characteristics of observational studies looking at associations of light intensity physical activity with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Aggio et al. (2016)[96]	Cross-sectional	70-92	1268	UK	ActiGraph GT3X: Time in LIPA (min/day)	EWGSOP	Grip strength	MAMC	Gait speed	Gait speed alone was positively related with the overall time spent in LIPA.
Bann et al. (2015)[78]	Cross-sectional	70-89	1130	USA	ActiGraph GT3X: Lower-light intensity PA (min/day); Higher-light intensity PA (min/day)	N/A	Grip strength	N/A	N/A	Higher-LIPA was positively associated with MS in men but not in women.
Sánchez-Sánchez et al. (2019)[64]	Cross-sectional	78.08 (5.71)	512	Spain	ActiGraph: LIPA (h/day)	FNIH	Grip strength	DXA	Gait speed	Only minor effects of LIPA on sarcopenia and its determinants were indicated.
Scott et al. (2020)[66]	Cross-sectional	70+	3334	Sweden	ActiGraph GT3X+: Total LIPA time (h)	EWGSOP2	Grip strength	iDXA	TUG	Higher volumes of LIPA were positively associated with MM and PP.

Abbreviations: DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; EWGSOP2: European Working Group on Sarcopenia in Older People 2; FNIH: Foundation for the National Institutes of Health; LIPA: light intensity physical activity; MAMC: mid-upper arm muscle circumference; MM: muscle mass; MS: muscle strength; N/A: Not available; PA: physical activity; PP: physical performance; SB: sedentary behavior; TUG: timed up and go test.

2.2.2.3 Moderate to Vigorous Intensity Physical Activity

Overview: Moderate to vigorous intensity physical activity (MVPA) is the merged term for the combination of moderate intensity PA which is equivalent to 3-5.9 METs and vigorous-intensity PA which corresponds to the equal or greater amount of 6 METs.[97] The 2018 Physical Activity Guidelines for Americans (PAG) suggests that people aged 65 and above should engage in a minimum of 150 minutes MVPA in order to improve overall health conditions.[59] A strong consensus among epidemiological experts can be found regarding the positive health benefits of MVPA on reducing all-cause mortality.[98] Nevertheless, there are still many unanswered questions regarding the association of MVPA on underlying health conditions including sarcopenia.

Study Outcomes Review: Based on our literature review, 6 articles examined the association of total MVPA volumes with defined sarcopenia and its parameters (Table 5). The majority of the collected studies implied significant relationship between high levels of MVPA and lower odds for a sarcopenic condition. Likewise, better physical performance measures were significantly correlated with high volumes of MVPA across all collected studies. While muscle strength also displayed a strong link with MVPA, muscle mass was inconsistently related with this metric. These findings suggest that MVPA in older adults may have a more potent impact on the maintenance of muscle strength and physical performance compared to muscle mass.

Participants with sarcopenia spent significantly less time in MVPA compared to their counterparts without sarcopenia.[66] Furthermore, the odds for a severe sarcopenia diagnosis were considerably lower among participants with higher daily volumes of MVPA even after adjusting for several confounding factors.[96] Within this framework,

substituting 1 hour of SB with 1 hour of MVPA per day was significantly related to better sarcopenia-relevant outcomes.[64] Scott et al.[66] estimated lower likelihoods of 20%, 12%, and 66% for diminished muscle strength, muscle mass and physical performance following an increment of 1 hour per week in MVPA, respectively. In conclusion, MVPA might play a role in the prevention of sarcopenia.

Table 5: Characteristics of observational studies looking at associations of moderate to vigorous intensity physical activity with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Aggio et al. (2016)[96]	Cross-sectional	70-92	1268	UK	ActiGraph GT3X: Time in MVPA (min/day)	EWGSOP	Grip strength	MAMC	Gait speed	MS and PP measures indicated a positive association with MVPA. Higher volumes of MVPA were also related with lower odds of severe sarcopenia.
Poyatos et al. (2016)[99]	Cross-sectional	65-79	36	Spain	ActiGraph GT3X: PA (min/day) divided into moderate and vigorous PA groups	N/A	Grip strength	N/A	N/A	A positive relationship between grip strength and MVPA in older women was reported.
Cooper et al. (2015)[100]	Cross-sectional	60-64	1727	UK	Actiheart: Time spent in MVPA (min/day)	N/A	Grip strength	N/A	RCS; Standing balance time; TUG speed	Significant associations of higher MVPA levels with better MS and several PP measures were pointed out.
Sánchez-Sánchez et al. (2019)[64]	Cross-sectional	78.08 (5.71)	512	Spain	ActiGraph: MVPA (h/day)	FNIH	Grip strength	DXA	Gait speed	Expanding the time spent in MVPA by 1 hour per day was significantly associated with a lower likelihood for sarcopenia and better MS, MM, and PP.

Scott et al. (2020)[66]	Cross-sectional	70+	3334	Sweden	ActiGraph GT3X+: Total MVPA time (h)	EWGSOP2	Grip strength	iDXA	TUG	Higher volumes of MVPA were significantly associated with probable or confirmed sarcopenia. All sarcopenia-relevant parameters were positively correlated with MVPA.
Westbury et al. (2018)[90]	Cross-sectional	74-84	131	UK	GENEactiv: Daily time spent in MVPA (≥ 100 mg)	EWGSOP	Grip strength	DXA	Gait speed	More time spent in MVPA demonstrated no association with sarcopenia and its components.

Abbreviations: BIA: bioelectrical impedance analysis; DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; EWGSOP2: European Working Group on Sarcopenia in Older People 2; FNIH: Foundation for the National Institutes of Health; MAMC: mid-upper arm muscle circumference; MM: muscle mass; MS: muscle strength; MVPA: moderate to vigorous physical activity; N/A: Not available; PA: physical activity; PP: physical performance; RCS: repeated chair stand test; TUG: timed up and go test.

2.2.2.4 Bouts of Physical Activity

Overview: Since the publication of the Physical Activity and Health recommendation by the Centers for Disease Control and Prevention and the American College of Sports Medicine in 1995,[101] MVPA bouts have been endorsed by PA epidemiologists over a period of more than 20 years.[102] At this point in time, intermittent bouts of 8 to 10 minutes MVPA were considered as health beneficial as long as the total volume of 30 minutes MVPA on preferably each day of the week was achieved.[101] The intention of including a PA bout suggestion was to encourage people to be more active by providing more flexibility regarding the accumulation of the recommended total volume of MVPA.[101]

In 2008, the recommendations created by the Physical Activity Guideline for Americans (PAG) concluded that MVPA bouts should be realized for at least 10 minutes in order to attain substantial health benefits.[60] The recommended guidance of performing MVPA bouts with a length of 10 minutes or longer was predominantly based on self-report studies.[102] The recently revised 2018 PAG excluded the recommended PA bouts of at least 10 minutes with the argument that free-living PA was mainly performed sporadically with a duration lower than 10 minutes.[62] Findings from a systematic review of cross-sectional and prospective cohort studies conducted by Jakicic et al.[62] indicated that any PA bout lower than 10 minutes was still related to better results in a variety of health-specific outcomes as long as the total recommended volume of PA was accumulated.

However, there is still a need to investigate and understand PA patterns of different target groups and their association with various health outcomes. These studies

may be particularly important for populations who have issues performing PA bouts longer than 10 minutes. According to research results from Saint-Maurice et al.[47], more than 30% of US adults older than 40 years of age produced zero PA bouts longer than 10 minutes. This proportion is expected to increase even further in the growing old-age population since the duration of PA bouts tend to decrease progressively with aging.[49]

In general, knowledge about the efficacy of PA bouts in comparison with the total volume of PA in older adults is still scarce.[63] Additionally, a better understanding of the relationship between the influence of various MVPA bout durations and health outcomes would enable better tailored and more effective PA recommendations for older adults.[103] Jefferis et al.[63] reported a significant association between accumulated sporadic MVPA bouts with periods of less than 10 minutes among older adults and a decreased risk of all-cause mortality. Another study indicated that older adults who achieved the PA guidelines showed higher muscle mass and physical function measures compared to inactive participants regardless of the type of accumulation, whether realized in short or in long bouts.[104]

Study Outcomes Review: Only one investigation provided information regarding the association of PA bouts with sarcopenia and its indicators (Table 6). Scott et al.[66] reported that the vast majority of various long MVPA bouts (≥10 minutes) was associated with lower odds for probable or confirmed sarcopenia and their components. Moreover, each LIPA bout duration from 10-19 minutes to ≥60 minutes indicated positive correlations with muscle mass and physical performance, but not with muscle strength.[66] Overall, these findings implied that various patterns of accumulated PA did not demonstrate different effects on sarcopenia and its indicators compared to the total

volume of PA.[66] Nevertheless, to the best of our knowledge, no study has investigated the association of PA bouts lower than 10 minutes with sarcopenia and its individual components yet.

Table 6: Characteristics of observational studies looking at associations of physical activity bouts with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Scott et al. (2020)[66]	Cross-sectional	70+	3334	Sweden	ActiGraph GT3X+: Total number of bouts for LIPA and MVPA	EWGSOP2	Grip strength	iDXA	TUG	The pattern in which PA was accumulated did not influence significant associations of the total volume of PA with sarcopenia and its parameters.

Abbreviations: DXA: dual-energy X-ray absorptiometry; EWGSOP2: European Working Group on Sarcopenia in Older People 2; LIPA: light intensity physical activity; MM: muscle mass; MS: muscle strength; MVPA: moderate to vigorous intensity physical activity; PP: physical performance; TUG: timed up and go test.

2.3 Association of Sedentary Behavior with Defined Sarcopenia and its Components among Older Adults

2.3.1 Self-report Measurement of Sedentary Behavior

Overview: Independent from PA, sedentary behavior (SB) reveals a negative impact on human health.[105] SB is defined as a waking activity which requires an energy expenditure of less than or equal to 1.5 METs.[105] The total daily amount of sedentary time may reach its peak at the older age range.[106] According to a systematic review published by Harvey et al.[107], accelerometer data demonstrated that 67% of the global old-age population remained sedentary for more than 8.5 hours per day. These overall high amounts of sitting time are associated with an increased risk for all-cause mortality as well as with chronic illnesses such as cardiovascular disease and type 2 diabetes.[108]

A total of 9 studies from our literature review were collected regarding the association of SB with defined sarcopenia and its indicators. Two studies applied self-report measures and 7 assessed SB with accelerometry. Notably, one study used a combination of self-report and accelerometer tools to evaluate sitting behavior. Similar to the PA measurement, the application of self-report methods to investigate the link between SB and health outcomes commonly leads to considerably underestimated outcomes which attenuates the internal validity of the study. On the other hand, in comparison to device-based assessments, self-report measures may be very useful for the gathering of contextual information such as type of performed SB.[109]

Study Outcomes Review: In sum, 2 studies applied self-report methods in order to evaluate the association of SB with defined sarcopenia and its determinants (Table 7). The cross-sectional analysis performed by Gianoudis et al.[45] indicated that an increment

of the total sitting time by 1 hour led to a 33% higher odds for sarcopenia. Higher levels of TV viewing, on the other hand, were related to lower leg muscle mass.[45] These study results imply that the impact on sarcopenic measures may vary based on the type of performed SB. A meta-analysis with data from more than 1 million participants showed that the effect of TV-viewing time was more strongly associated with all-cause mortality than the daily sitting time.[110] Plausible reasons for this difference might be the lack of sedentary breaks and common dietary behaviors during TV viewing.[110,111] In this context, TV viewing time might also have a more adverse influence on muscle strength, muscle mass, and physical performance than other types of SB.

Table 7: Characteristics of observational studies looking at associations of self-report sedentary behavior with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Bann et al. (2015)[78]	Cross-sectional	70-89	1130	USA	CHAMPS	N/A	Grip strength	N/A	N/A	Total SB time was not associated with grip strength.
Gianoudis et al. (2015)[45]	Cross-sectional	60-86	162	Australia	CHAMPS	EWGSOP	Knee extensor strength	DXA	RCS; Four square step test; TUG	Each 1-hour more of total sitting time per day was related with higher odds of sarcopenia. Higher TV viewing times were linked with lower leg lean mass.

Abbreviations: CHAMPS: Community Healthy Activities Model Program for Seniors; DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; MM: muscle mass; MS: muscle strength; N/A: Not available; PP: physical performance; RCS: repeated chair stand test; SB: sedentary behavior; TUG: timed up and go test.

2.3.2 Objective Measurement of Sedentary Behavior

Overview: In epidemiological research, the device-based assessment of SB is considered as the more valid and reliable method in a free-living environment compared to self-report measurements.[112] The ActiGraph GT3X is a primarily energy-expenditure algorithm driven instrument.[112] This wearable device can use a specific threshold of activity counts which should reflect energy expenditure levels of less than 1.5 METs in order to define SB.[112] The activPAL, on the other hand, focuses on physical position measurements.[112] Both devices induce bias owing to the misclassification of SB.[112] For instance, ActiGraphs are less able to differentiate between postures since they fully focus on the intensity of movements.[113] Thus, activities of LIPA are commonly misclassified as SB and vice versa because standing positions usually fall below the determined activity counts threshold.[113] In contrast, activPALs which have set their main focus on posture are incapable of finding differences between SB and active sitting or lying with MET values of more than 1.5 such as several forms of weightlifting.[112]

While energy-expenditure driven tools such as the ActiGraph may provide more valid outcomes of PA, the application of posture-directed devices such as the activPAL are more accurate in terms of assessing SB.[112,114] Despite their limitations, both accelerometers can provide a relatively good estimation of SB volumes and patterns.[113] This enables investigators to get a better picture of behavioral patterns and thus of how and when sitting time is accumulated each day.[108]

2.3.2.1 Total Volume of Sedentary Behavior

Study Outcomes Review: Overall, 7 investigations employed accelerometry to estimate the association of the total volume of SB with defined sarcopenia and its components (Table 8). In the majority of the collected studies, the significance of the associations of defined sarcopenia, muscle strength and muscle mass with the total volume of SB was lacking. However, physical performance seemed to be affected by the total time spent in SB since most of the studies displayed a significant relationship. These study results indicate the potentially positive effect of reducing SB on preserving physical function among older adults.

Table 8: Characteristics of observational studies looking at associations of total volume of sedentary behavior with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Aggio et al. (2016)[96]	Cross-sectional	70-92	1268	UK	ActiGraph GT3X: SB time (min/day)	EWGSOP	Grip strength	MAMC	Gait speed	Lower gait speed was associated with more time spent in SB.
Bann et al. (2015)[78]	Cross-sectional	70-89	1130	USA	ActiGraph GT3X: SB time (min/day)	N/A	Grip strength	N/A	N/A	Grip strength suggested no relationship with the total volume SB.
Cooper et al. (2015)[100]	Cross-sectional	60-64	1727	UK	Actiheart: Time spent sedentary (hours/day)	N/A	Grip strength	N/A	RCS; Standing balance time; TUG speed	Lower MS and TUG time were correlated with higher volumes of SB.
Reid et al. (2018)[115]	Cross-sectional	65-84	123	Australia	activPAL3: Total SB (h/day)	EWGSOP and FNIH	Knee extensor strength	DXA	Four square step test; RCS; TUG; Gait speed	MM was negatively associated with higher levels of SB.

Rojer et al. (2018)[91]	Cross-sectional	74.4 (72.4 - 78.0)	80	Netherlands	DynaPort MoveMonitor: Inactive duration (h/day); Mean duration of inactive periods (minutes/period)	N/A	Grip strength	BIA	Gait speed	Worse gait speed measures were correlated with higher volumes of SB.
Sánchez-Sánchez et al. (2019)[64]	Cross-sectional	78.08 (5.71)	512	Spain	ActiGraph: SB (h/day); LIPA (h/day)	FNIH	Grip strength	DXA	Gait speed	Each 1-hour increase of total SB was associated with higher odds of sarcopenia.
Scott et al. (2020)[66]	Cross-sectional	70+	3334	Sweden	ActiGraph GT3X+: Total SB (h)	EWGSOP2	Grip strength	iDXA	TUG	The total volume of SB was negatively associated with PP.

Abbreviations: BIA: bioelectrical impedance analysis; DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; EWGSOP2: European Working Group on Sarcopenia in Older People 2; FNIH: Foundation for the National Institutes of Health; MAMC: mid-upper arm muscle circumference; MM: muscle mass; MS: muscle strength; N/A: Not available; PP: physical performance; RCS: repeated chair stand test; SB: sedentary behavior; TUG: timed up and go test.

2.3.2.2 Bouts and Breaks in Sedentary Time

Overview: While a bout of SB is characterized as an interval of uninterrupted sitting time, sedentary breaks are described as the PA time of any intensity between two sedentary bouts.[108] Independent of the total time spent in SB, specific sedentary patterns such as breaking up sedentary time every 20 minutes have been shown to provide favorable effects on postprandial glucose and insulin levels in overweight or obese adults.[116] Overall, better metabolic health measures have been reported in participants who exhibited shorter sedentary bouts with a higher frequency of sitting breaks compared to those who produced prolonged SB with less breaks.[117] Therefore, investigations in the growing elderly community may be even more important since daily sedentary bouts tend to increase in length with aging.[48]

Study Outcomes Review: According to our literature search, 3 studies investigated the association of sedentary bouts or breaks with defined sarcopenia and its determinants (Table 9). Overall, sedentary breaks indicated non-significant associations with defined sarcopenia. The correlation between breaks in sedentary time and sarcopenia-related parameters was analyzed in 2 investigations. Only physical performance was positively linked with sedentary breaks based on the cross-sectional analysis from Aggio et al.[96]. However, Reid et al.[115] concluded a lack of significance regarding this relationship. In addition, another study examined the correlation of sitting bouts with sarcopenic indicators. Scott et al.[66] pointed out that each sedentary period which lasted longer than 20 minutes was related with worse outcomes of physical performance. Muscle strength as well as muscle mass, on the contrary, were not associated with any reported sedentary bout.

Table 9: Characteristics of observational studies looking at associations of sedentary bouts and breaks with defined sarcopenia and/or sarcopenia-relevant metrics

Study Characteristics					Exposure Information	Outcome Information				Findings
Study	**Study Design**	**Age**	**Sample Size**	**Country**	**Measurement Tool**	**Sarcopenia Definition**	**MS Measure**	**MM Measure**	**PP Measure**	**Main Findings**
Aggio et al. (2016)[96]	Cross-sectional	70-92	1268	UK	ActiGraph GT3X: Breaks in sedentary time per hour	EWGSOP	Grip strength	MAMC	Gait speed	Sedentary breaks were positively related with PP.
Reid et al. (2018)[115]	Cross-sectional	65-84	123	Australia	activPAL3: Sit-to-stand transition/day	EWGSOP and FNIH	Knee extensor strength	DXA	Four square step test; RCS; TUG; Gait speed	Breaks of SB implied no correlations with all sarcopenia-relevant parameters after adjusting for various confounding factors.
Scott et al. (2020)[66]	Cross-sectional	70+	3334	Sweden	ActiGraph GT3X+: Total number of bouts for SB	EWGSOP2	Grip strength	iDXA	TUG	Only TUG time as a measure of PP was positively related with sedentary bouts.

Abbreviations: DXA: dual-energy X-ray absorptiometry; EWGSOP: European Working Group on Sarcopenia in Older People; EWGSOP2: European Working Group on Sarcopenia in Older People 2; FNIH: Foundation for the National Institutes of Health; MAMC: mid-upper arm muscle circumference; MM: muscle mass; MS: muscle strength; PP: physical performance; RCS: repeated chair stand test; SB: sedentary behavior; TUG: timed up and go test.

2.3.2.3 Activity Fragmentation

Overview: Epidemiological research shows that the activity profile changes substantially with aging by displaying shorter PA bouts[118] and longer bouts of SB.[119] Older adults often have difficulty sustaining PA for an extended period of time.[48–50] This may lead to a frequent compensatory interchange of PA and SB during a day.[48] Frequent transition states between a minute-by-minute captured sedentary and active behavior via accelerometry indicate a higher PA fragmentation which have been previously shown to be associated with worse health status in older adults.[48–51]

To the best of our knowledge, only one study has looked at the associations of activity fragmentation with sarcopenia and its indicators.[45] However, physical behavior metrics were assessed via self-report in this study which may have diminished the validity of the calculated activity fragmentation.[45] An investigative approach of applying accelerometry to identify the association of activity fragmentation with sarcopenia status and its parameters is missing. Activity fragmentation can be estimated with the active-to-sedentary transition probability (ASTP) index which is calculated by dividing the number of PA bouts with the sum of minutes spent in PA (Figure 5).[48] Utilizing the active-to-sedentary transition probability (ASTP) index in epidemiological studies might enable researchers to obtain a more profound understanding of fragmented activity patterns among oldest-old adults which may present crucial insights into age-related muscle changes.

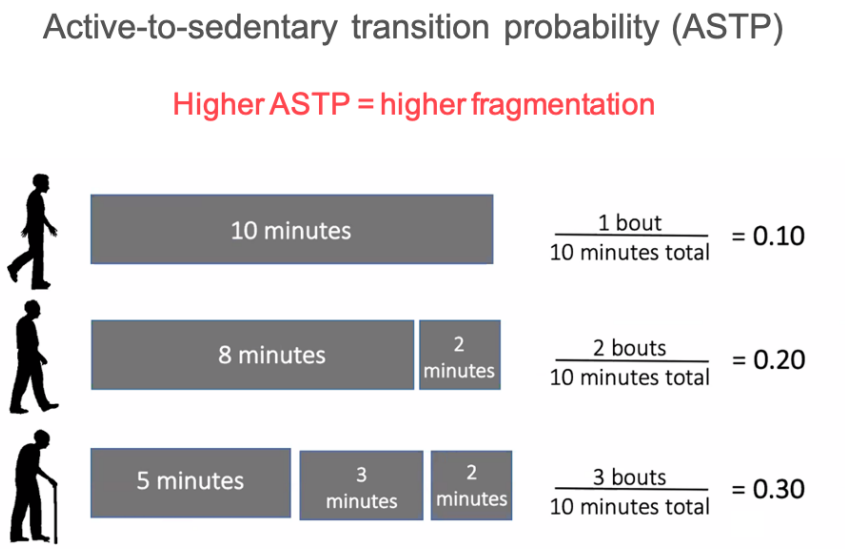

Figure 6: Calculation of the activity-to-sedentary transition probability. Figure provided by Jennifer A. Schrack, PhD.

2.4. Strengths and Limitations of Applying Subjective- and Objective Measurement Methods in Studies with Older Adults

As previously indicated, selecting the appropriate measurement tool to evaluate PA or SB in a free-living environment is an important component of the research methodology with pivotal consequences on the validity and reliability of the study outcomes. Prior to choosing a suitable measure of PA or SB, imperative attributes such as the evidence-based quality of each methodological approach and the benefit-cost analysis should be considered.[71] Study characteristics, population characteristics, instrument characteristics, and activity characteristics are factors to contemplate when selecting the best possible method of activity evaluation.[88] The most commonly used approach to assess PA in epidemiological research is still the self-report questionnaire.[120] Questionnaires are described as valuable and cost-effective instruments to measure various types of PA, whether these activities are performed statically, such as weightlifting, or dynamically, such as walking.[70] In addition, owing to their simple

operationality for responder and respondent, subjective measures are advantageous in studies with large sample sizes as well as long time periods.[70]

However, PA is highly complex and consists of a broad activity spectrum regarding the volume and intensity.[58] This multicomponent shape of PA leads involuntarily to an incidental recall bias and thus to an over- or underestimation of the test results which is caused by the inability of self-report questionnaires to obtain precise minute-by-minute measures.[121] Similar to that, SB measures assessed via subjective methods also commonly experience underestimation of the true study outcomes.[122]

Accelerometry, on the other hand, can translate body acceleration counts into measures of energy expenditure.[70] The correct utilization of accelerometers enables investigators to collect more accurate information on the volume and frequency of various intensities.[70] However, activities such as different forms of strength training or cycling are often not accurately detected by accelerometry.[70]

Strengths and limitations of PA measurement methodologies also vary between the differences of population attributes, including age, gender, body weight, or co-morbid conditions, which lead to even more pronounced difficulties of selecting an effective and accurate assessment method.[71] For instance, activity patterns experience substantial changes across the life course with overall steady decreases of PA levels from young to old.[118] Due to commonly diminished physical functions or multimorbid conditions, older adults show large dissimilarities regarding the type and intensity of PA compared to the younger population.[123] In this regard, older adults usually exhibit high levels of LIPA such as casual walking or different types of household tasks which may be difficult to

capture via self-report questionnaires owing to their incorrect conceptualization of this intensity range.[124]

Additionally, most of the self-report assessments substantially underestimate the actual levels of SB and frequently record only about a half of the accelerometer measurements among older adults.[125] The application of accelerometry in old-age population studies helped alleviating parts of the issues by being able to collect low activity levels and by limiting recall bias.[124]

However, the variety of accelerometer types and the different data collection and processing criteria provides challenges for researchers to select the best possible device for measuring PA and SB. Age-specific data collection protocols such as device placement or sampling frequency as well as data processing criteria such as filters, epoch length, non-wear time definition, cut-points, and algorithms are imperative settings which need to be carefully considered.[89] In this regard, the misclassification of behavioral activities in which most accelerometers exhibit limited functional abilities to differentiate between SB and LIPA is considered as a huge limitation of objective measurements.[112] For instance, while the activPAL as a posture-focused device may ignore active sitting such as weightlifting, the ActiGraph as an energy expenditure-prone wearable may disregard passive standing.[112,126]

2.5 Literature Review Summary

The broad spectrum of activity behavior in terms of length, intensity, and frequency seems to influence sarcopenia and its components including muscle strength, muscle mass, and physical performance. Our systematic literature review implied positive associations of LIPA with physical performance. In this context, LIPA might become

more important with advancing age since low intensities can be endured for a longer period of time and are easier to perform with higher frequencies during a day. Higher volumes of LIPA also lead to a considerable reduction of SB and its potentially associated negative consequences on muscle health.

MVPA seems to be the most effective type of intensity to reduce the odds of sarcopenia according to our systematic literature search. Implementing higher levels of MVPA in daily routines may be essential for lowering the risk of a sarcopenia diagnosis. However, as previously discussed, MVPA may be difficult to sustain for long time periods by older adults. Accumulated activity bouts with time periods of less than 10 minutes seem to be understudied despite their common presence throughout day-to-day activity patterns among the old-age population. To the best of our knowledge, no study has investigated the association of short sporadic activity bouts (<10 minutes) with defined sarcopenia and its individual components. Identifying this relationship via observational studies may fill a valuable gap in geriatric research.

In contrast to the mainly positive effects of PA, SB shows rather adverse implications on sarcopenia-related physical performance measures. Long sedentary bouts and short sitting breaks presented an inverse relationship with physical performance among older adults. Notably, insufficient information was available regarding the association of activity fragmentation with sarcopenia and its parameters. The activity fragmentation might indicate a useful marker for deteriorated muscle health among older adults.

Across the study outcomes of our literature review, higher volumes of PA and lower volumes of SB were associated with better physical performance regardless of the

provided bout length and intensity. Engaging in activities with higher intensity might play a role to obtain an additional positive effect on muscle strength and mass and thus lower the odds for sarcopenia. Short MVPA bouts (<10 minutes), which might be better achievable for older adults, may provide enough stimuli to the muscles in order to lower the odds of sarcopenia and to improve sarcopenia-relevant parameters. In summary, investigating the relationship between the whole spectrum of activity behavior and sarcopenia among older adults provides huge opportunities to address this growing geriatric health issue.

CHAPTER 3

METHODS

3.1 Introduction

This secondary analysis will evaluate associations of accelerometer-measured PA patterns and total volume of PA with EWGSOP2 defined sarcopenia and its indicators, including muscle strength, muscle mass, and physical performance, among oldest-old adults. Cross-sectional cohort data from the Health, Aging, and Body Composition (Health ABC) study helps address this research question. The Health ABC study is an observational investigation with the main purpose of collecting information on a multitude of risk factors, encompassing weight-related health conditions and behavioral determinants which may lead to functional decline and loss of independence among healthy community-dwelling older adults. Their valuable data collection of measurements on body composition, strength and function as well as accelerometer-assessed PA in a sample of oldest-old adults contributes to the realization of our defined investigative aims.[67]

3.2 Participants

A study cohort composed of 3075 community-dwelling black and white men and women aged 70-79 years at baseline were randomly recruited from the metropolitan areas of Memphis, TN and Pittsburgh, PA. Participants were excluded from the study if they demonstrated: 1.) difficulties to walk one quarter of a mile or to climb 10 steps without resting; 2.) difficulties with instrumental activities of daily living; 3.) a history of cancer treatment in the last 3 years; 4.) a plan to move out of the geographic study area in the

next 3 years. Baseline data of clinical assessments as well as home interviews were gathered between April 1997 and June 1998. All recruited participants were followed for a total of 16 years with various subjective and objective evaluations each year. Written informed consent was given from each involving study subject. Furthermore, the institutional review boards from the University of Tennessee and the University of Pittsburgh approved the investigation.

Cross-sectional data from year 16 was used for this analysis due to the availability of measures of muscle strength, body composition, physical performance, and accelerometry. The primary sample was analyzed for associations of various behavior metrics, including total activity counts, total moderate to vigorous physical activity (MVPA) time, total light intensity physical activity (LIPA) time, total sedentary behavior (SB) time, total short MVPA bouts (<10 minutes) duration, total long MVPA bouts (≥10 minutes) duration, total number of sedentary breaks, and the active-to-sedentary transition probability (ASTP), with handgrip strength only, which is stated as the main indicator of sarcopenia and allows the definition of a probable sarcopenic state according to the EWGSOP2.[18] One-hundred forty-seven participants from the Memphis, TN and Pittsburgh, PA region were included in the primary sample which was based on the availability of handgrip strength data tested on both hands and valid accelerometer measures recorded for at least 4 days.[127]

As reported by EWGSOP2, confirmed sarcopenia is specified as a combination of low handgrip strength and low appendicular lean mass. An additional detection of low gait speed measures concludes a severe sarcopenic condition.[18] Consequently, a subsample of the primary samples was created which required valid data of handgrip

strength, appendicular lean mass, gait speed, and accelerometry. A total of 87 participants located in the Memphis area were available for the subsample analysis. The subsample was used to examine the relationships of various physical behavior metrics with probable, confirmed, and severe sarcopenia and their individual components including handgrip strength, appendicular lean mass, and gait speed.

3.3 Study Protocol

3.3.1 Sarcopenia-Related Metrics

3.3.1.1 Muscle Strength

Upper limb muscle strength was measured with the help of an isometric hand-held dynamometer (Jaymar, JLW Instruments, Chicago, IL) for handgrip strength. The test was conducted two times for each hand with the mean of all four evaluations used for the analysis. Participants who reported severe hand pain or recent surgery were excluded from the study.

3.3.1.2 Muscle Mass

Total fat mass and appendicular lean mass were evaluated using whole body DXA (Hologic QDR 4500, software version 8.21, Bedford, MA) scans which were solely performed in Memphis and included as part of the subsample examination. The appendicular lean mass was quantified by summarizing the lean mass in arms and legs.

3.3.1.3 Physical Performance

Gait speed was applied as a measurement of physical performance among the sample of oldest-old adults. In this regard, a 20-meter course marked by an orange cone

at the end of the track was created. Participants were instructed to walk along the course with their usual pace from a specified starting point to the orange cone. The timer was started when the participant crossed the starting line and was stopped following the first step after the finish line. Moreover, the usage of walking aids, such as a cane or walkers, were allowed during the evaluation process.

3.3.2 Physical Activity Assessment

3.3.2.1 Accelerometry

Participants were instructed to wear an ActiGraph GT3X+ accelerometer (ActiGraph, Pensacola, Florida, USA) on their right hip for 7 consecutive days. The monitors were worn during all waking hours except water-related activities such as swimming and taking a bath or a shower. In addition, participants were instructed to take off the device prior to sleep time and put it back on after getting up in the morning. Three-axis acceleration data in free-living conditions were captured by applying 1 second epoch periods. The analog acceleration signals were digitized by a 12-bit Analog to Digital Converter with the sampling frequency of 80 Hertz and passed through a digital filter that band limits the accelerometer to the frequency range of 0.25 to 2.5 Hertz in order to efficiently detect human motions. Afterwards, movement data from all eligible participants were uploaded to the ActiLife software (Version 6.5.1; ActiGraph, Pensacola, FL, USA) to manage and analyze the collected information.

3.3.3 Covariates

Demographic factors, including age, gender, race, and education level, were identified with an interviewer-administered questionnaire at study baseline. Body mass

index (BMI) data was calculated by taking the body weight (kg) and dividing by the height (meters) squared. A calibrated standard balance beam scale and a Harpenden stadiometer (Holtain Ltd, Crosswell, UK) were applied to measure the weight and height, respectively. Smoking status was the only measure determined at year 1 and was included as a covariate in our study since a previous meta-analysis has shown that cigarette smoking might contribute to the development of sarcopenia.[128] Accelerometer wear time was quantified as described in Chapter 3.3.2.1. Furthermore, the prevalence of physician-diagnosed chronic conditions, including diabetes, hypertension, history of cardiovascular disease, and history of cancer, were also included as potential confounders to the analysis. These data were ascertained by algorithms based on self-reports and medication use.

3.4 Data Analysis

3.4.1 Primary Outcome

Sarcopenia was our primary outcome of interest. Sarcopenic indicators included muscle strength, muscle mass, and physical performance measures.[2] Cut points for sarcopenia-associated parameters were provided by the revised definition of the European Working Group on Sarcopenia in Older People 2 (EWGSOP2)[18]. Probable, confirmed, or severe sarcopenia were defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (handgrip strength: <27 kg for men and <16 kg for women), low muscle mass tested by a Dual-energy X-ray absorptiometry (appendicular lean mass: <20 kg for men and <15 kg for women), and low physical performance assessed by a 20-m usual walking speed test (gait speed: ≤0.8 m/s).[18] We examined each

sarcopenic condition as a dichotomous variable and each sarcopenia-related metric as a continuous variable.

3.4.2 Primary Exposures

3.4.2.1 Physical Behavior Volume Metrics

The total volume of various physical behavior metrics including sedentary behavior (SB), light intensity physical activity (LIPA), and moderate to vigorous intensity physical activity (MVPA) were determined using the ActiGraph GT3X+ accelerometer data. We identified the total minutes of PA per day (at any bout length) of total activity counts, LIPA, MVPA, and SB. The classification of the overall time spent in different physical behavior intensities was determined using counts per minute (cpm) intensity threshold values. In this context, SB was categorized as <100 cpm,[129] LIPA was categorized as 100-1040 cpm,[130] and MVPA was categorized as ≥1041 cpm.[130] Participants were excluded from the study when they did not provide ≥4 days of valid accelerometer data of 10 hours per day.[127]

3.4.2.2 Physical Behavior Pattern Metrics

We examined MVPA split into bouts lasting <10 minutes and ≥10 minutes. This enabled us to compare the efficacy of short MVPA bouts (<10 minutes) and long MVPA bouts (≥10 minutes) with the total volume of MVPA on EWGSOP2 defined sarcopenia and its components. The selected duration of these 10 minute intensity bouts was based on the PA recommendations imposed by the PAG 2008 and the World Health Organization.[60,61] Furthermore, although bouts were removed in the most recent 2018

PAG,[59] there is a need for future research to understand how the accumulation of PA influences health outcomes.[62]

We investigated the associations of the total number of sedentary breaks and activity fragmentation with sarcopenic status and its components. A sedentary break was registered when participants provided ≥100 cpm for at least 1 minute following a sedentary bout. The activity fragmentation was quantified with the active-to-sedentary transition probability (ASTP) index. This index gave us an estimation of the fragmentation level of the provided PA patterns. ASTP was computed for each day and averaged across valid days to derive a single measure for each participant.[48] To calculate activity fragmentation in Health ABC, we used the number of breaks in SB divided by the total sum of minutes spent in PA. Higher activity fragmentation represents more interruptions in activity.

3.5 Statistical Analyses

Participant characteristics comprised of baseline demographic data (age, gender, race, and education level) and at the year 16 visit accelerometer measures of physical behavior metrics as well as year 16 visit sarcopenia-related metrics were summarized and expressed as mean (standard deviation) or median (interquartile range) for continuous variables or as frequency and percentage for categorical variables. Differences of participant baseline characteristics by sarcopenic status were determined by independent samples t-tests or Mann-Whitney U tests for continuous variables and chi-square tests for categorical variables.

For each analysis described below we used the following variables as primary exposures: total activity counts, total MVPA time (min/day), total LIPA time (min/day),

total SB time (min/day), total MVPA minutes in short bouts (<10 minutes in duration; min/day), total MVPA minutes in long bouts (≥10 minutes in duration; min/day), total number of sedentary breaks (number of breaks/day), and ASTP (number of sedentary breaks / total PA time).

Multivariate linear regression models were employed to determine the cross-sectional association of each PA variable with sarcopenia-relevant indicators as continuous variables including handgrip strength, appendicular lean mass, and gait speed. In order to evaluate the odds for EWGSOP2 defined probable, confirmed, and severe sarcopenia diagnosis, binomial logistic regression models were used. This provided clinical relevance since we were able to understand whether sarcopenia as our primary outcome is associated with distinct PA behaviors and patterns. The odds of probable, confirmed, and severe sarcopenia were estimated for incrementally higher levels of total activity counts, total MVPA time (per 5 min/day), total LIPA time (per 60 min/day), total SB time (per 60 min/day), total MVPA <10 minute bout duration (per 5 min/day), total MVPA ≥10 minutes bout duration (per 5 min/day), total number of sedentary breaks (per 1 number of sedentary breaks/day), and ASTP (per 0.1 ASTP).

These linear and logistic regression models were adjusted for age, gender, race, education, and accelerometer wear time in model 1. In model 2, we adjusted for the covariates presented in model 1 plus lifestyle factors including BMI and smoking status. Model 3 provided adjustments for all covariates presented in model 2 plus chronic health conditions including diabetes, hypertension, history of cardiovascular disease, and history of cancer.

We also examined the dose-response associations of the total volume of PA and PA patterns on EWGSOP2 defined probable sarcopenia, confirmed sarcopenia, and severe sarcopenia among this oldest-old adult population sample. This provided crucial information on the linearity or non-linearity of the relationships and whether threshold levels exist for activity behaviors in association with sarcopenia status. Dose-response associations of behavioral activity metrics, including total activity counts, total MVPA time (min/day), total LIPA time (min/day), total SB time (min/day), total MVPA <10 minute bout duration (min/day), total MVPA ≥10 minute bout duration (min/day), total number of sedentary breaks (number of breaks/day), and ASTP (number of sedentary breaks / total PA time), with EWGSOP2 defined probable sarcopenia, confirmed sarcopenia, and severe sarcopenia were evaluated. Categorical variables were created for each PA metric by dividing them into tertiles or groups. Participants were allocated in three equally sized tertiles based on their level of total activity counts, total LIPA time, total SB time, total MVPA <10 bout duration, total number of sedentary breaks, and ASTP. The first (lowest) tertile was considered the reference group. For the total volume of MVPA, three groups were generated in which 0-5 minutes represented the first group, 5-10 minutes the second group, and ≥10 minute the third group in order to draw a clearer picture of the statistical results. Due to the expected low presence of the overall minutes spent in any long MVPA bouts (≥10 minute) among oldest-old adults, participants were either administered to the group which provided not a single long MVPA bout period or to the group with at least some amount of long MVPA bout duration.

A two-tailed hypothesis testing with an alpha level of 0.05 proved statistical significance of these examinations. All data were analyzed and illustrated using the statistical software R-studio (R Foundation for Statistical Computing, Vienna, Austria).

CHAPTER 4

RESULTS

4.1 Primary Sample

4.1.1 Participant Characteristics

The primary sample included 145 participants with valid handgrip strength and at least 4 days of 10 hours per day of accelerometer wear. One participant was excluded due to irregularly high acceleration counts, likely caused by accelerometer malfunction. Table 10 presents characteristics of the final 145 participants. Fifty-two (35.9%) individuals were categorized as probable sarcopenic based on the applied EWGSOP2 criteria. The mean age was 88.2 (2.5) years and 81 (55.9%) were women, 45 (31.0%) were black race, and 92 (63.4%) individuals completed a postsecondary degree. Participants spent on average 9.6 (10.4) minutes per day or 1.1% (1.2%) of the accelerometer wear time in MVPA, 151.3 (58.7) minutes per day or 18.0% (7.1%) in LIPA, and 686.6 (128.0) minutes per day or 80.8% (7.8%) in SB. The mean handgrip strength of men was 28.2 (6.3) kg and for women 18.0 (5.1) kg. Significant differences in handgrip strength between the nonsarcopenic group (men: 32.5 (4.6) kg; women: 20.5 (3.6) kg) and probable sarcopenic group (men: 22.8 (3.4); women: 12.2 (3.2) kg) were identified. In addition, significant differences were found among the data of education level, race, total time spent in MVPA, total time spent in MVPA bouts of <10 minutes, and total time spent in MVPA bouts of ≥10 minutes. However, no differences between groups regarding the average minutes of accelerometer wear time, total activity counts, LIPA, SB, number of sedentary breaks, and ASTP were discovered.

Table 10: Participant characteristics of the primary sample

	Total sample (n = 145)	Nonsarcopenic (n = 93)	Probable sarcopenic (n = 52)	p-value for difference
Demographic factors				
Age, years, mean (SD)	88.2 (2.5)	88.2 (2.7)	88.3 (2.3)	0.75
Women, n (%)	81 (55.9%)	57 (61.3%)	24 (46.2%)	0.11
Race, n (%), black	45 (31.0%)	35 (37.6%)	10 (19.2%)	**0.03**
Education, n (%), postsecondary	92 (63.4%)	57 (61.3%)	35 (67.3%)	**<0.01**
Site, n (%), Memphis	103 (71.0%)	67 (72.0%)	36 (69.2%)	0.87
Lifestyle factors				
BMI (kg/m2), mean (SD)	27.1 (4.6)	27.52 (4.7)	26.2 (4.5)	0.10
Current smoker, n (%)	4 (2.8%)	2 (2.2%)	2 (3.8%)	0.95
Chronic health conditions				
Diabetes, n (%)	40 (27.6%)	26 (28.0%)	14 (26.9%)	1.00
Hypertension, n (%)	109 (75.2%)	70 (75.3%)	39 (75.0%)	1.00
History of cardiovascular disease, n (%)	50 (34.5 %)	33 (35.5%)	17 (32.7%)	0.88
History of cancer, n (%)	42 (29.0%)	29 (31.2%)	13 (25.0%)	0.55
Muscle strength				
Handgrip strength (kg), mean (SD)	22.5 (7.6)	25.1 (7.1)	17.9 (6.3)	**<0.01**
Handgrip strength men (kg), mean (SD)	28.2 (6.3)	32.5 (4.6)	22.8 (3.4)	**<0.01**
Handgrip strength women (kg), mean (SD)	18.0 (5.1)	20.5 (3.6)	12.2 (3.2)	**<0.01**
Accelerometer				
Average minutes of weartime (min/day), mean (SD)	847.6 (119.8)	837.5 (107.7)	865.6 (138.0)	0.21
TAC (counts/day), mean (SD)	244,233 (104,544)	248,011 (107,972)	237,475 (98,779)	0.55
% time MVPA, median (IQR)	0.7 (0.3, 1.6)	0.9 (0.4, 1.9)	0.5 (0.3, 1.0)	**<0.01**
% time MVPA, mean (SD)	1.1 (1.2)	1.3 (1.3)	0.8 (1.0)	**<0.01**
% LIPA, mean (SD)	18.0 (7.1)	18.7 (7.1)	16.9 (6.8)	0.14
% SB, mean (SD)	80.8 (7.8)	80.0 (7.9)	82.4 (7.3)	0.08

MVPA (min/day), median (IQR)	5.7 (3.2, 13.2)	6.5 (3.3, 15.7)	3.9 (2.3, 8.0)	**<0.01**
MVPA (min/day), mean (SD)	9.6 (10.4)	11.1 (11.0)	6.9 (8.6)	**<0.01**
LIPA (min/day), mean (SD)	151.3 (58.7)	154.8 (57.3)	145.2 (61.3)	0.36
SB (min/day), mean (SD)	686.6 (128.0)	671.6 (121.7)	713.5 (135.6)	0.07
MVPA in bouts <10 min (min/day), median (IQR)	5.4 (3.2, 10.9)	6.4 (3.3, 13.8)	3.9 (2.3, 8.0)	**<0.01**
MVPA in bouts <10 min (min/day), mean (SD)	8.5 (8.8)	9.6 (8.9)	6.6 (8.3)	**<0.01**
MVPA in bouts ≥10 min (min/day), median (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	**<0.01**
MVPA in bouts ≥10 min (min/day), mean (SD)	1.1 (3.2)	1.5 (3.8)	0.3 (1.5)	**<0.01**
Number of sedentary breaks (No. of breaks/day), mean (SD)	69.5 (18.9)	69.5 (15.6)	69.4 (23.8)	0.99
ASTP, mean (SD)	0.47 (0.11)	0.46 (0.12)	0.49 (0.10)	0.12

Notes: Bold values are significant. All data are mean +/- SD (independent samples t tests), except median (interquartile range) (Mann-Whitney U tests) and proportions (chi-square test). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.

Abbreviations: ASTP: active-to-sedentary transition probability; BMI: body mass index; LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; SB: sedentary behavior; TAC: Total activity counts.

4.1.2 Associations of Physical Behavior Metrics with Probable Sarcopenia (Binomial Logistic Regressions)

Volumes: Table 11 presents the odds ratios for the associations of physical behavior volume metrics with probable sarcopenia determined by EWGSOP2. After adjusting for age, gender, race, education, and accelerometer wear time (model 1), each 5 minute higher per day of MVPA was related with a 28% (95% CI 0.57 to 0.92) lower likelihood for probable sarcopenia. This association remained significant following further adjustments for lifestyle factors including BMI and smoking status (OR=0.73, 95% CI 0.58 to 0.92, model 2) as well as chronic health conditions such as diabetes, hypertension, cardiovascular disease, and cancer (OR=0.73, 95% CI 0.57 to 0.92, model 3). There were no significant associations of total activity counts, LIPA, and SB with probable sarcopenia.

Table 11: Odds ratios for the associations of physical behavior volume metrics with probable sarcopenia

	Dichotomous (yes/no) Probable sarcopenic *OR (95% CI)*
Physical behavior volumes	
TAC (per 1 SD (104,544 counts))	
Model 1	0.79 (0.54 to 1.18)
Model 2	0.78 (0.52 to 1.16)
Model 3	0.77 (0.51 to 1.15)
Total MVPA (per 5 minutes higher)	
Model 1	**0.72 (0.57 to 0.92)**
Model 2	**0.73 (0.58 to 0.92)**
Model 3	**0.73 (0.57 to 0.92)**
Total LIPA (per 60 minutes higher)	
Model 1	0.81 (0.55 to 1.19)
Model 2	0.83 (0.56 to 1.22)
Model 3	0.82 (0.55 to 1.21)
Total SB (per 60 minutes higher)	
Model 1	1.30 (0.91 to 1.84)
Model 2	1.27 (0.89 to 1.81)
Model 3	1.28 (0.89 to 1.84)

Notes: Bold values are significant. Probable sarcopenia is defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women).
Abbreviations: LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval); SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Patterns: Regarding the associations of physical behavior pattern metrics with probable sarcopenia in Table 12, we found that 5 minutes per day higher levels of short MVPA bouts (<10 minutes) were associated with 27% (95% CI 0.56 to 0.96) lower odds for a probable sarcopenia diagnosis in the final adjusted model. For longer MVPA bouts (≥10 minutes), each 5 minute more per day demonstrated a 69% (95% CI 0.10 to 0.95) lower likelihood for probable sarcopenia after final adjustment. Sedentary breaks and ASTP were not associated with probable sarcopenia.

Table 12: Odds ratios for the associations of physical behavior pattern metrics with probable sarcopenia

	Dichotomous (yes/no) Probable sarcopenic *OR (95% CI)*
Physical behavior patterns	
MVPA <10 minute bouts (per 5 minutes higher)	
Model 1	**0.73 (0.56 to 0.95)**
Model 2	**0.74 (0.57 to 0.96)**
Model 3	**0.73 (0.56 to 0.96)**
MVPA ≥10 minute bouts (per 5 minutes higher)	
Model 1	**0.30 (0.10 to 0.91)**
Model 2	**0.30 (0.10 to 0.94)**
Model 3	**0.31 (0.10 to 0.95)**
Number of sedentary breaks (No. of breaks/day)	
Model 1	1.00 (0.98 to 1.02)
Model 2	1.00 (0.98 to 1.02)
Model 3	1.00 (0.98 to 1.02)
ASTP (per 0.1 ASTP)	
Model 1	1.29 (0.94 to 1.79)
Model 2	1.26 (0.91 to 1.74)
Model 3	1.25 (0.90 to 1.73)

Notes: Bold values are significant. Probable sarcopenia is defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval).
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

4.1.3 Associations of Physical Behavior Metrics with Handgrip Strength (Multivariate Linear Regressions by Gender)

Applying multivariate linear regressions by gender among the primary sample (Table 13 and Table 14) provided no statistically significant association of any physical behavior volume or pattern variable with handgrip strength.

Table 13: Linear regression associations of physical behavior volume metrics with handgrip strength by gender

	Handgrip strength (kg) *ß (95% CI)*	
	Men (n = 64)	Women (n = 81)
Physical behavior volumes		
TAC (per 1 SD (104,544 counts))		
Model 1	0.69 (-0.84 to 2.22)	0.59 (-0.63 to 1.82)
Model 2	0.91 (-0.67 to 2.49)	0.62 (-0.62 to 1.86)
Model 3	0.71 (-0.86 to 2.27)	0.41 (-0.91 to 1.72)
Total MVPA (per 5 minutes higher)		
Model 1	0.53 (-0.09 to 1.14)	0.63 (-0.04 to 1.30)
Model 2	0.58 (-0.04 to 1.20)	0.58 (-0.10 to 1.28)
Model 3	0.45 (-0.16 to 1.07)	0.57 (-0.13 to 1.28)
Total LIPA (per 60 minutes higher)		
Model 1	0.04 (-1.50 to 1.58)	0.98 (-0.24 to 2.20)
Model 2	0.13 (-1.43 to 1.69)	0.93 (-0.33 to 2.18)
Model 3	0.18 (-1.39 to 1.74)	0.70 (-0.66 to 2.06)
Total SB (per 60 minutes higher)		
Model 1	-0.24 (-1.62 to 1.13)	-0.95 (-2.06 to 0.15)
Model 2	-0.34 (-1.73 to 1.06)	-0.90 (-2.04 to 0.24)
Model 3	-0.33 (-1.72 to 1.07)	-0.72 (-1.95 to 0.52)

Notes: Bold values are significant.
Abbreviations: ß (95% CI): Beta coefficient (95% confidence interval); LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Table 14: Linear regression associations of physical behavior pattern metrics with handgrip strength by gender

	Handgrip strength (kg) *ß (95% CI)*	
	Men (n = 64)	Women (n = 81)
Physical behavior patterns		
MVPA <10 minute bouts (per 5 minutes higher)		
Model 1	0.47 (-0.30 to 1.23)	0.65 (-0.08 to 1.38)
Model 2	0.55 (-0.23 to 1.33)	0.61 (-0.14 to 1.35)
Model 3	0.46 (-0.30 to 1.23)	0.57 (-0.20 to 1.34)
MVPA ≥10 minute bouts (per 5 minutes higher)		
Model 1	1.68 (-0.01 to 3.37)	2.25 (-1.55 to 6.06)
Model 2	1.67 (-0.03 to 3.37)	2.09 (-1.83 to 6.01)
Model 3	1.14 (-0.58 to 2.86)	2.70 (-1.30 to 6.70)
Number of sedentary breaks (No. of breaks/day)		
Model 1	-0.01 (-0.09 to 0.06)	0.08 (0.00 to 0.15)
Model 2	-0.01 (-0.09 to 0.07)	0.08 (0.00 to 0.15)
Model 3	-0.01 (-0.09 to 0.06)	-0.01 (-0.01 to 0.15)
ASTP (per 0.1 ASTP)		
Model 1	-0.31 (-1.74 to 1.13)	-0.49 (-1.46 to 0.47)
Model 2	-0.37 (-1.82 to 1.08)	-0.42 (-1.43 to 0.58)
Model 3	-0.33 (-1.78 to 1.12)	-0.33 (-1.28 to 0.87)

Notes: Bold values are significant. The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; ß (95% CI): Beta coefficient (95% confidence interval); MVPA: moderate to vigorous physical activity.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

4.1.4 Dose-Response Associations of Physical Behavior Metrics with Probable Sarcopenia

Volumes: Dose-response associations of physical behavior volume metrics with the odds of probable sarcopenia specified by EWGSOP2 are presented in Table 15. Participants who accumulated at least 10 minutes of total MVPA had 26% (95% CI 0.62 to 0.89) lower odds of probable sarcopenia compared to the reference group of participants accumulating less than 5 minutes per day of total MVPA volumes in the fully adjusted model. There were no significant associations across tertiles of total activity counts, LIPA, and SB with probable sarcopenia.

Table 15: Dose-response associations of physical behavior volume metrics with probable sarcopenia

Dose-response associations of TAC tertiles with probable sarcopenia

	Total TAC (mean/SD)		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
TAC, mean (SD)	144,307 (43,221)	232,572 (21,296)	357,901 (85,911)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.02 (0.84 to 1.24)	0.90 (0.74 to 1.10)
Model 2	Ref	1.01 (0.84 to 1.23)	0.89 (0.73 to 1.09)
Model 3	Ref	1.01 (0.83 to 1.23)	0.88 (0.71 to 1.08)

Dose-response associations of total MVPA groups with probable sarcopenia

	Total MVPA (min/day)		
	0-5 min Group	5-10 min Group	≥10 min Group
n	67	34	44
MVPA, mean (SD)	2.7 (1.1)	7.1 (1.4)	21.9 (11.1)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.91 (0.76 to 1.11)	**0.73 (0.61 to 0.88)**
Model 2	Ref	0.92 (0.76 to 1.11)	**0.74 (0.62 to 0.89)**
Model 3	Ref	0.91 (0.75 to 1.12)	**0.74 (0.62 to 0.89)**

Dose-response associations of total LIPA tertiles with probable sarcopenia

	Total LIPA (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
LIPA, mean (SD)	92.2 (29.3)	148.7 (13.4)	214.3 (42.5)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.96 (0.80 to 1.17)	0.90 (0.74 to 1.09)
Model 2	Ref	0.96 (0.80 to 1.17)	0.91 (0.75 to 1.11)
Model 3	Ref	0.97 (0.80 to 1.18)	0.91 (0.74 to 1.11)

Dose-response associations of total SB tertiles with probable sarcopenia

	Total SB (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
SB, mean (SD)	577.4 (54.1)	662.7 (21.6)	822.0 (122.3)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.02 (0.83 to 1.24)	1.20 (0.93 to 1.53)
Model 2	Ref	1.03 (0.84 to 1.26)	1.21 (0.94 to 1.55)
Model 3	Ref	1.02 (0.83 to 1.25)	1.21 (0.94 to 1.57)

Notes: Bold values are significant. Probable or confirmed sarcopenia will be defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women).
Abbreviations: LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval); Ref: Reference; SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Patterns: Table 16 illustrates dose-response associations of physical behavior pattern metrics with the odds of probable sarcopenia defined by EWGSOP2 in the primary sample. The highest tertile of accumulated minutes in short MVPA bouts of less than 10 minutes also demonstrated a 22% (95% CI 0.64 to 0.95) lower likelihood for probable sarcopenia, compared to the lowest tertile of short MVPA bouts (<10 minutes) following final adjustment. Likewise, the odds of probable sarcopenia were 22% (95% CI 0.63 to 0.98, model 3) lower among participants who had any minutes spent in long MVPA bouts of at least 10 minutes compared to participants who had zero accumulated time in long MVPA bouts (≥10 minutes). The study results also indicated no significant associations across tertiles of sedentary breaks and ASTP with probable sarcopenic status.

Table 16: Dose-response associations of physical behavior pattern metrics with probable sarcopenia

Dose-response associations of short MVPA bouts (<10 minutes) duration tertiles with probable sarcopenia

	MVPA <10 minute bout (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
MVPA <10 minute bout, mean (SD)	2.2 (0.9)	5.6 (9.5)	17.8 (9.8)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.90 (0.75 to 1.09)	**0.77 (0.63 to 0.93)**
Model 2	Ref	0.89 (0.74 to 1.08)	**0.77 (0.64 to 0.94)**
Model 3	Ref	0.89 (0.74 to 1.08)	**0.78 (0.64 to 0.95)**

Dose-response associations of long MVPA bouts (≥10 minutes) duration groups with probable sarcopenia

	MVPA ≥10 minute bout (min/day)	
	No ≥10 minute bouts	≥10 minute bouts
n	124	21
MVPA ≥10 minute bout, mean (SD)	0.0 (0.0)	7.3 (5.3)
Probable sarcopenia (yes/no)		
Model 1	Ref	**0.77 (0.62 to 0.96)**
Model 2	Ref	**0.78 (0.62 to 0.97)**
Model 3	Ref	**0.78 (0.63 to 0.98)**

Dose-response associations of number of sedentary breaks tertiles with probable sarcopenia

	Number of sedentary breaks (no. of breaks/day)		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
Sedentary breaks, mean (SD)	50.4 (12.4)	70.2 (3.8)	88.2 (13.4)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.04 (0.86 to 1.26)	0.92 (0.76 to 1.13)
Model 2	Ref	1.04 (0.86 to 1.26)	0.92 (0.75 to 1.12)
Model 3	Ref	1.03 (0.85 to 1.26)	0.91 (0.74 to 1.12)

Dose-response associations of ASTP tertiles with probable sarcopenia

	ASTP		
	First Tertile	Second Tertile	Third Tertile
n	49	48	48
ASTP, mean (SD)	0.35 (0.05)	0.47 (0.03)	0.59 (0.07)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.15 (0.94 to 1.40)	1.21 (1.00 to 1.47)
Model 2	Ref	1.14 (0.94 to 1.38)	1.19 (0.98 to 1.45)
Model 3	Ref	1.14 (0.93 to 1.40)	1.18 (0.97 to 1.44)

Notes: Bold values are significant. Probable sarcopenia is defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval); Ref: Reference.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

4.2 Subsample

4.2.1. Participant Characteristics

The subsample included 87 participants with valid measurements of handgrip strength, DXA scans, gait speed, and accelerometry. Among them, 28 (32.2%) were classified as probable sarcopenic, 18 (20.7%) as confirmed sarcopenic, and 8 (9.2%) as severe sarcopenic according to the EWGSOP2 definition. The demographic and lifestyle factors of our subsample revealed mean values or frequencies similar to the primary sample. On average, participants in the subsample spent 9.1 (10.7) minutes per day or 1.1% (1.2%) of the accelerometer wear time in MVPA, 148.4 (54.0) minutes per day or 17.9% (6.9%) in LIPA, and 684.3 (139.4) minutes per day or 81.0% (7.7%) in SB. The mean of sarcopenia-relevant metrics, including handgrip strength (men: 29.2 (6.6) kg, women: 18.4 (5.5) kg), appendicular lean mass (men: 21.6 (2.7) kg, women: 15.3 (2.9) kg), and gait speed (0.96 (0.24) m/s), are reported in Table 17.

Table 17: Participant characteristics of the subsample

	Total sample (n = 87)	Nonsarcopenic (n = 59)	Probable sarcopenic (n = 28)	Confirmed sarcopenic (n = 18)	Severe sarcopenic (n = 8)
Demographic factors					
Age, years, mean (SD)	88.2 (2.5)	88.2 (2.8)	88.4 (2.0)	87.9 (2.1)	87.9 (1.6)
Women, n (%)	48 (55.2%)	34 (57.6%)	14 (50.0%)	11 (61.1%)	5 (62.5%)
Race, n (%), black	27 (31.0%)	23 (39.0%)	4 (14.3%)	3 (16.7%)	2 (25.0%)
Education, n (%), postsecondary	53 (60.9%)	34 (57.6%)	19 (67.9%)	14 (77.8%)	6 (75.0%)
Site, n (%), Memphis	87 (100.0%)	59 (100.0%)	28 (100.0%)	18 (100.0%)	8 (100.0%)
Lifestyle factors					
BMI (kg/m2), mean (SD)	26.6 (4.3)	27.3 (4.6)	25.2 (3.3)	24.1 (3.2)	24.4 (3.6)
Current smoker, n (%)	4 (4.6%)	2 (3.4%)	2 (7.1%)	2 (11.1%)	1 (12.5%)
Chronic health conditions					
Diabetes, n (%)	20 (23.0%)	13 (22.0%)	7 (25.0%)	5 (27.8%)	3 (37.5%)
Hypertension, n (%)	63 (72.4%)	41 (69.5%)	22 (78.6%)	15 (83.3%)	8 (100.0%)
History of cardiovascular disease, n (%)	28 (32.2%)	19 (32.2%)	9 (32.1%)	5 (27.8%)	4 (50.0%)
History of cancer, n (%)	27 (31.0%)	20 (33.9%)	7 (25.0%)	3 (16.7%)	2 (25.0%)
Muscle strength					
Handgrip strength (kg), mean (SD)	23.3 (8.0)	26.1 (7.2)	17.2 (6.0)	15.8 (6.2)	16.9 (5.5)
Handgrip strength men (kg), mean (SD)	29.2 (6.6)	33.1 (4.2)	22.3 (3.3)	22.1 (3.9)	22.8 (3.0)
Handgrip strength women (kg), mean (SD)	18.4 (5.5)	21.0 (3.9)	12.1 (3.0)	11.8 (3.3)	13.3 (2.4)
DXA-acquired body composition measures					
Total body fat (%), mean (SD)	34.8 (6.7)	35.1 (6.9)	34.3 (6.2)	35.9 (5.5)	36.2 (4.4)
Appendicular lean mass (kg), mean (SD)	18.1 (4.2)	18.8 (4.1)	16.7 (4.0)	14.9 (3.2)	15.0 (3.2)
Appendicular lean mass men (kg), mean (SD)	21.6 (2.7)	22.4 (2.8)	20.2 (2.0)	18.6 (0.9)	18.7 (0.9)

Appendicular lean mass women (kg), mean (SD)	15.3 (2.9)	16.2 (2.8)	13.2 (1.8)	12.5 (1.1)	12.7 (0.5)
Physical performance					
Gait speed (m/s), mean (SD)	0.96 (0.24)	1.00 (0.24)	0.90 (0.23)	0.85 (0.23)	0.63 (0.10)
Accelerometer					
Average minutes of weartime (min/day), mean (SD)	841.8 (126.7)	840.2 (124.2)	845.3 (134.1)	835.1 (101.0)	814.1 (110.4)
TAC (counts/day), mean (SD)	245,687 (109,216)	248,125 (115,022)	240,549 (97,635)	225,578 (96,781)	203,376 (137,803)
% time MVPA, median (IQR)	0.6 (0.3, 1.1)	0.7 (0.4, 1.7)	0.4 (0.3, 1.0)	0.4 (0.1, 0.8)	0.3 (0.2, 0.4)
% time MVPA, mean (SD)	1.1 (1.2)	1.2 (1.3)	0.8 (1.1)	0.6 (0.5)	0.4 (0.3)
% LIPA, mean (SD)	17.9 (6.9)	18.5 (7.2)	16.7 (6.2)	14.9 (5.5)	12.9 (5.7)
% SB, mean (SD)	81.0 (7.7)	80.2 (8.1)	82.5 (6.8)	84.5 (5.7)	86.7 (5.8)
MVPA (min/day), median (IQR)	4.9 (3.0, 11.3)	5.2 (3.2, 14.9)	3.4 (2.8, 7.4)	3.5 (3.0, 6.8)	3.0 (1.7, 3.5)
MVPA (min/day), mean (SD)	9.1 (10.7)	10.3 (11.2)	6.6 (9.2)	4.9 (3.6)	3.0 (2.0)
LIPA (min/day), mean (SD)	148.4 (54.0)	153.0 (57.0)	138.6 (46.5)	123.1 (41.2)	104.7 (45.8)
SB (min/day), mean (SD)	684.3 (139.4)	676.9 (139.8)	700.0 (139.8)	707.2 (106.8)	706.4 (110.5)
MVPA in bouts <10 min (min/day), median (IQR)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
MVPA in bouts <10 min (min/day), mean (SD)	8.0 (8.7)	8.7 (8.5)	6.6 (9.2)	4.9 (3.6)	3.0 (2.0)
MVPA in bouts ≥10 min (min/day), median (IQR)	4.9 (3.0, 9.6)	5.2 (3.2, 12.3)	3.4 (2.8, 7.4)	3.5 (3.0, 6.8)	3.0 (1.7, 3.5)
MVPA in bouts ≥10 min (min/day), mean (SD)	1.1 (3.7)	1.6 (4.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Number of sedentary breaks (No. of breaks/day), mean (SD)	70.4 (17.0)	70.9 (17.2)	69.4 (16.9)	63.9 (15.9)	60.1 (20.8)
ASTP, mean (SD)	0.48 (0.12)	0.48 (0.13)	0.50 (0.09)	0.52 (0.09)	0.58 (0.08)

Notes: All data are mean +/- SD (independent samples t tests), except median (interquartile range) (Mann-Whitney U-tests) and proportions (chi-square test). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; BMI: body mass index; LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; SB: sedentary behavior**;** TAC: Total activity counts.

4.2.2 Associations of Physical Behavior Metrics with Sarcopenia Status (Binomial Logistic Regressions)

Volumes: Table 18 demonstrates the odds ratios for the associations of physical behavior volume metrics with any sarcopenic status according to the EWGSOP2 definition, including probable sarcopenia, confirmed sarcopenia, and severe sarcopenia, in the subsample.

Probable sarcopenia: There were no significant associations of any physical behavior volume metric with probable sarcopenia.

Confirmed sarcopenia: Each 5 minutes per day of MVPA higher was associated with a 49% (95% CI 0.26 to 0.98) lower likelihood for confirmed sarcopenia after adjusting for age, gender, race, education, and accelerometer wear time (model 1). Similarly, each 60 minutes higher of daily LIPA was associated with 55% (95% CI 0.22 to 0.89) lower odds of confirmed sarcopenia in the same model (model 1). However, the associations of LIPA and MVPA with confirmed sarcopenia were attenuated and thus no longer significant after further adjusting for lifestyle factors (model 2) and chronic health conditions (model 3). Furthermore, each additional 60 minutes per day of SB volume was associated with 2.1 (95% CI 1.01 to 4.35) times higher odds of confirmed sarcopenia after full adjustment. No significant association was observed between total activity counts and confirmed sarcopenia.

Severe sarcopenia: The odds for a severe sarcopenia diagnosis were 68% (95% CI 0.11 to 0.91, model 2) lower following each 60 minutes more per day of LIPA but did not remain significant after full adjustment (model 3). Each additional 60 minutes per day spent in SB was associated with 3.18 (95% CI 1.13 to 8.92, model 2) times higher odds

of severe sarcopenia. However, the significance of this relationship was also attenuated and therefore no longer significant after adjusting for chronic health conditions (model 3). In addition, there were no significant associations of total activity counts and MVPA with severe sarcopenia.

Table 18: Odds ratios for the associations of physical behavior volume metrics with sarcopenia status

	Dichotomous (yes/no)		
	Probable sarcopenic *OR (95 % CI)*	Confirmed sarcopenic *OR (95% CI)*	Severe sarcopenic *OR (95% CI)*
Physical behavior volumes			
TAC (per 1 SD (109,216 counts))			
Model 1	0.84 (0.51 to 1.38)	0.65 (0.34 to 1.24)	0.54 (0.21 to 1.43)
Model 2	0.82 (0.49 to 1.36)	0.64 (0.33 to 1.26)	0.53 (0.19 to 1.47)
Model 3	0.85 (0.49 to 1.46)	0.57 (0.27 to 1.21)	0.54 (0.17 to 1.70)
Total MVPA (per 5 minutes higher)			
Model 1	0.74 (0.54 to 1.02)	**0.51 (0.26 to 0.98)**	0.10 (0.01 to 1.13)
Model 2	0.75 (0.54 to 1.02)	0.52 (0.26 to 1.02)	0.06 (0.00 to 1.10)
Model 3	0.75 (0.54 to 1.05)	0.48 (0.23 to 1.00)	0.02 (0.00 to 1.17)
Total LIPA (per 60 minutes higher)			
Model 1	0.77 (0.45 to 1.32)	**0.45 (0.22 to 0.89)**	**0.30 (0.11 to 0.82)**
Model 2	0.83 (0.48 to 1.43)	0.50 (0.24 to 1.03)	**0.32 (0.11 to 0.91)**
Model 3	0.89 (0.49 to 1.58)	0.47 (0.21 to 1.04)	0.27 (0.07 to 1.07)
Total SB (per 60 minutes higher)			
Model 1	1.35 (0.82 to 2.20)	**2.19 (1.15 to 4.18)**	**3.23 (1.23 to 8.47)**
Model 2	1.27 (0.77 to 2.08)	**1.99 (1.01 to 3.89)**	**3.18 (1.13 to 8.92)**
Model 3	1.20 (0.71 to 2.02)	**2.10 (1.01 to 4.35)**	3.79 (0.99 to 14.56)

Notes: Bold values are significant. Probable or confirmed sarcopenia will be defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women), low muscle mass tested by a dual-energy X-ray absorptiometry (appendicular skeletal muscle mass: <20 kg for men and <15 kg for women), and low physical performance assessed by a 20-m usual walking speed test (gait speed: ≤0.8 m/s).
Abbreviations: LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval); SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Patterns: Table 19 shows the odds ratios for the associations of physical behavior pattern metrics with any sarcopenic status according to the EWGSOP2 definition,

including probable sarcopenia, confirmed sarcopenia, and severe sarcopenia, in the subsample.

Probable sarcopenia: All physical behavior pattern metrics, including short MVPA bouts (<10 minutes), long MVPA bouts (≥10 minutes), total number of sedentary breaks, and ASTP, showed non-significant associations with probable sarcopenia.

Confirmed sarcopenia: There were no significant associations of any physical behavior pattern metric with confirmed sarcopenia.

Severe sarcopenia: Each 0.1 ASTP higher was associated with 2.9 (95% CI 1.05 to 8.02) times higher odds of severe sarcopenia in the fully adjusted model 3. Other PA pattern metrics, including short MVPA bouts (<10 minutes), long MVPA bouts (≥10 minutes), and sedentary breaks, were not associated with severe sarcopenia.

Table 19: Odds ratios for the associations of physical behavior pattern metrics with sarcopenia status

	Dichotomous (yes/no)		
	Probable sarcopenic *OR (95 % CI)*	Confirmed sarcopenic *OR (95% CI)*	Severe sarcopenic *OR (95% CI)*
Physical behavior patterns			
MVPA <10 minute bouts (per 5 minutes higher)			
Model 1	0.80 (0.57 to 1.12)	0.49 (0.24 to 1.00)	0.09 (0.01 to 1.02)
Model 2	0.80 (0.57 to 1.11)	0.51 (0.25 to 1.05)	0.05 (0.00 to 1.00)
Model 3	0.81 (0.57 to 1.15)	0.47 (0.22 to 1.01)	0.02 (0.00 to 1.09)
MVPA ≥10 minute bouts (per 5 minutes higher)			
Model 1	N/A	N/A	N/A
Model 2	N/A	N/A	N/A
Model 3	N/A	N/A	N/A
Number of sedentary breaks (No. of breaks/day)			
Model 1	1.00 (0.97 to 1.03)	0.97 (0.94 to 1.00)	0.96 (0.92 to 1.01)
Model 2	1.00 (0.97 to 1.03)	0.97 (0.94 to 1.01)	0.96 (0.92 to 1.01)
Model 3	1.01 (0.97 to 1.04)	0.97 (0.93 to 1.01)	0.96 (0.91 to 1.02)
ASTP (per 0.1 ASTP)			
Model 1	1.27 (0.84 to 1.91)	1.51 (0.94 to 2.43)	**2.30 (1.17 to 4.50)**
Model 2	1.23 (0.81 to 1.87)	1.50 (0.89 to 2.50)	**2.47 (1.19 to 5.15)**
Model 3	1.16 (0.75 to 1.80)	1.43 (0.82 to 2.48)	**2.90 (1.05 to 8.02)**

Notes: Bold values are significant. Probable or confirmed sarcopenia will be defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women), low muscle mass tested by a dual-energy X-ray absorptiometry (appendicular skeletal muscle mass: <20 kg for men and <15 kg for women), and low physical performance assessed by a 20-m usual walking speed test (gait speed: ≤0.8 m/s). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval).
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

4.2.3 Associations of Physical Behavior Metrics with Sarcopenia-Relevant Components (Multivariate Linear Regressions by Gender)

Volumes: Table 20 illustrates multivariate linear regression outcomes by gender of the subsample on associations of physical behavior volume metrics with sarcopenia-related parameters including handgrip strength, appendicular lean mass, and gait speed.

Handgrip strength: There were no significant associations of handgrip strength with any physical behavior volume metric in the subsample.

Appendicular lean mass: Among women, each 60 minutes per day higher SB was associated with lower appendicular lean mass (ß=-0.66, 95% CI -1.31 to -0.01) after adjusting for age, gender, race, education, and accelerometer wear time (model 1) but did not remain significant after further adjustments for lifestyle factors (model 2) and chronic health conditions (model 3). Total activity counts, LIPA, and MVPA were not associated with appendicular lean mass in women. Men demonstrated non-significant associations across all physical behavior volume metrics, including total activity counts, MVPA, LIPA, and SB, with appendicular lean mass.

Gait speed: Gait speed was significantly better among men for each SD (109,216 counts) higher total activity counts (ß=0.09, 95% CI 0.01 to 0.17), each 5 minutes higher MVPA (ß=0.03, 95% CI 0.01 to 0.06), and each 60 minutes higher LIPA (ß=0.15, 95% CI 0.06 to 0.24) across all models. Higher volumes of SB demonstrated a non-significant association with gait speed in men. Among women, higher total activity counts per 1 SD (109,216 counts) showed associations with better gait speed in model 2 (ß=0.07, 95% CI 0.01 to 0.14) but lacked significance in model 3. Likewise, each 60 minutes more in LIPA was associated with higher gait speed (ß=0.12, 95% CI 0.05 to 0.18, model 2) and every 60 minutes more in SB was associated with lower gait speed (ß=-0.10, 95% CI -0.16 to -0.04, model 2) in women but did not remain significant after full adjustment. Total volumes of MVPA were not associated with gait speed among women.

Table 20: Linear regression associations of physical behavior volume metrics with sarcopenia-relevant components by gender

	Handgrip strength (kg) *ß (95% CI)*		Appendicular lean mass (kg) *ß (95% CI)*		Gait speed (m/s) *ß (95% CI)*	
	Men (n = 39)	Women (n = 48)	Men (n = 39)	Women (n = 48)	Men (n = 39)	Women (n = 48)
Physical behavior volumes						
TAC (per 1 SD (109,216 counts))						
Model 1	0.64 (-1.64 to 2.91)	0.33 (-1.23 to 1.90)	0.08 (-0.86 to 1.02)	0.36 (-0.37 to 1.08)	**0.09 (0.02 to 0.16)**	**0.07 (0.01 to 0.14)**
Model 2	0.71 (-1.63 to 3.05)	0.34 (-1.15 to 1.82)	0.36 (-0.45 to 1.16)	0.36 (-0.18 to 0.90)	**0.09 (0.02 to 0.16)**	**0.07 (0.01 to 0.14)**
Model 3	0.03 (-2.30 to 2.35)	-0.26 (-1.93 to 1.41)	0.17 (-0.65 to 0.99)	0.33 (-0.30 to 0.95)	**0.09 (0.01 to 0.17)**	0.03 (-0.04 to 0.10)
Total MVPA (per 5 minutes higher)						
Model 1	0.59 (-0.22 to 1.41)	0.53 (-0.61 to 1.68)	-0.04 (-0.39 to 0.30)	0.24 (-0.30 to 0.77)	**0.03 (0.01 to 0.06)**	0.04 (-0.01 to 0.09)
Model 2	0.60 (-0.22 to 1.43)	0.34 (-0.76 to 1.44)	-0.01 (-0.31 to 0.28)	0.07 (-0.34 to 0.48)	**0.03 (0.01 to 0.06)**	0.04 (-0.01 to 0.09)
Model 3	0.36 (-0.46 to 1.19)	0.13 (-1.07 to 1.34)	-0.04 (-0.34 to 0.25)	0.03 (-0.43 to 0.49)	**0.03 (0.01 to 0.06)**	0.01 (-0.04 to 0.06)
Total LIPA (per 60 minutes higher)						
Model 1	-0.12 (-2.93 to 2.69)	0.92 (-0.64 to 2.48)	0.03 (-1.13 to 1.18)	0.75 (0.04 to 1.45)	**0.13 (0.04 to 0.21)**	**0.11 (0.05 to 0.17)**
Model 2	-0.08 (-2.95 to 2.79)	0.50 (-1.04 to 2.04)	0.25 (-0.74 to 1.24)	0.39 (-0.17 to 0.95)	**0.13 (0.04 to 0.21)**	**0.12 (0.05 to 0.18)**
Model 3	-0.81 (-3.96 to 2.06)	-0.10 (-1.90 to 1.71)	0.35 (-0.66 to 1.37)	0.37 (-0.31 to 1.05)	**0.15 (0.06 to 0.24)**	0.07 (0.00 to 0.15)
Total SB (per 60 minutes higher)						
Model 1	-0.31 (-2.65 to 2.04)	-0.84 (-2.27 to 0.58)	0.01 (-0.96 to 0.97)	**-0.66 (-1.31 to -0.01)**	-0.11 (-0.18 to 0.04)	**-0.10 (-0.16 to -0.04)**
Model 2	-0.34 (-2.73 to 2.05)	-0.46 (-1.87 to 0.95)	-0.16 (-0.99 to 0.66)	-0.33 (-0.85 to 0.18)	-0.11 (-0.18 to 0.04)	**-0.10 (-0.16 to -0.04)**
Model 3	0.31 (-2.09 to 2.71)	0.06 (-1.59 to 1.71)	-0.21 (-1.06 to 0.63)	-0.31 (-0.93 to 0.31)	-0.13 (-0.20 to 0.05)	-0.06 (-0.13 to 0.00)

Notes: Bold values are significant.
Abbreviations: ß (95% CI): Beta coefficient (95% confidence interval); LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Patterns: Table 21 depicts multivariate linear regression outcomes by gender of the subsample on associations of physical behavior pattern metrics with sarcopenia-related indicators including handgrip strength, appendicular lean mass, and gait speed.

Handgrip strength: There were no significant associations of handgrip strength with any physical behavior pattern metric in the subsample.

Appendicular lean mass: A higher number of sedentary breaks was associated with higher appendicular lean mass (ß=0.05, 95% CI 0.01 to 0.09) among women in the fully adjusted model. There were no significant associations of short MVPA bouts (<10 minutes), long MVPA bouts (≥10 minutes), and ASTP with appendicular lean mass in women. On the other hand, all analyzed PA pattern metrics, including short MVPA bouts (<10-minutes), long MVPA bouts (≥10 minutes), sedentary breaks, and ASTP, showed non-significant associations with appendicular lean mass among men.

Gait speed: Each additional 5 minutes spent in short MVPA bouts (<10 minutes) among men was associated with faster gait speed in model 2 (ß=0.04, 95% CI 0.01 to 0.07) but attenuated after final adjustment. No relationship was observed between higher levels of short MVPA bouts (<10 minutes) and gait speed among women. Furthermore, men and women significantly lowered gait speed per each added 0.1 ASTP (men: ß=-0.14, 95% CI -0.20 to -0.08, women: ß=-0.07, 95% CI -0.12 to -0.02) in the fully adjusted model. On the other hand, long MVPA bouts (≥10 minutes) and sedentary breaks were not associated with gait speed in men and women.

Table 21: Linear regression associations of physical behavior pattern metrics with sarcopenia-relevant components by gender

	Handgrip strength (kg) *ß (95% CI)*		Appendicular lean mass (kg) *ß (95% CI)*		Gait speed (m/s) *ß (95% CI)*	
	Men (n = 39)	Women (n = 48)	Men (n = 39)	Women (n = 48)	Men (n = 39)	Women (n = 48)
Physical behavior patterns						
MVPA <10 minute bouts (per 5 minutes higher)						
Model 1	0.51 (-0.52 to 1.54)	0.56 (-0.62 to 1.74)	-0.04 (-0.47 to 0.39)	0.23 (-0.33 to 0.78)	**0.04 (0.01 to 0.07)**	0.05 (0.00 to 0.10)
Model 2	0.54 (-0.52 to 1.59)	0.44 (-0.68 to 1.57)	0.06 (-0.31 to 0.43)	0.12 (-0.29 to 0.54)	**0.04 (0.01 to 0.07)**	0.05 (0.00 to 0.11)
Model 3	0.30 (-0.73 to 1.34)	0.19 (-1.06 to 1.45)	0.01 (-0.36 to 0.38)	0.08 (-0.40 to 0.56)	0.00 (0.00 to 0.08)	0.02 (-0.03 to 0.07)
MVPA ≥10 minute bouts (per 5 minutes higher)						
Model 1	N/A	N/A	N/A	N/A	N/A	N/A
Model 2	N/A	N/A	N/A	N/A	N/A	N/A
Model 3	N/A	N/A	N/A	N/A	N/A	N/A
Number of sedentary breaks (No. of breaks/day)						
Model 1	-0.07 (-0.21 to 0.06)	0.07 (-0.03 to 0.16)	0.01 (-0.05 to 0.07)	**0.07 (0.03 to 0.11)**	0.00 (0.00 to 0.01)	0.01 (0.00 to 0.01)
Model 2	-0.07 (-0.21 to 0.07)	0.04 (-0.05 to 0.13)	0.02 (-0.03 to 0.07)	**0.05 (0.02 to 0.08)**	0.00 (0.00 to 0.01)	0.01 (0.00 to 0.01)
Model 3	-0.10 (-0.23 to 0.04)	0.01 (-0.10 to 0.11)	0.02 (-0.03 to 0.07)	**0.05 (0.01 to 0.09)**	0.00 (0.00 to 0.01)	0.00 (0.00 to 0.01)
ASTP (per 0.1 ASTP)						
Model 1	-0.02 (-2.13 to 2.09)	-0.60 (-1.86 to 0.65)	0.35 (-0.51 to 1.21)	-0.39 (-0.97 to 0.19)	**-0.12 (-0.17 to -0.06)**	**-0.10 (-0.14 to -0.05)**
Model 2	-0.04 (-2.19 to 2.10)	-0.36 (-1.58 to 0.86)	0.23 (-0.51 to 0.97)	-0.18 (-0.63 to 0.27)	**-0.12 (-0.18 to -0.06)**	**-0.10 (-0.15 to -0.05)**
Model 3	0.46 (-1.72 to 2.64)	-0.00 (-1.37 to 1.36)	0.06 (-0.72 to 0.83)	-0.17 (-0.69 to 0.35)	**-0.14 (-0.20 to -0.08)**	**-0.07 (-0.12 to -0.02)**

Notes: Bold values are significant. The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.

Abbreviations: ß (95% CI): ASTP: active-to-sedentary transition probability; Beta coefficient (95% confidence interval); MVPA: moderate to vigorous physical activity; N/A: Not available.

Model 1: adjusted for age, gender, race, education, accelerometer wear time

Model 2: model 1 + lifestyle factors (BMI, smoking status)

Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

4.2.4 Dose-Response Associations of Physical Behavior Metrics with Sarcopenia Status

Volumes: The outcomes of the subsample regarding the dose-response associations of physical behavior volume metrics with EWGSOP2 defined sarcopenic status, including probable sarcopenia, confirmed sarcopenia, and severe sarcopenia, are illustrated in Table 22.

Probable sarcopenia: In contrast to individuals who provided 0-5 minutes per day of total volume of MVPA, participants with at least 10 minutes per day of total MVPA showed significant lower odds of probable sarcopenia (OR=0.77, 95% CI 0.61 to 0.98, model 2). There were no significant associations across tertiles of total activity counts, LIPA, and SB with probable sarcopenia.

Confirmed sarcopenia: Participants in the highest tertile of total activity counts had significantly lower odds of confirmed sarcopenia (OR=0.81, 95% CI 0.66 to 0.99, model 2) when compared to participants in the lowest tertile. Model 1 and model 3 presented non-significant results of this association. The likelihood for a confirmed sarcopenia diagnosis was significantly lower among participants who spent at least 10 minutes per day in total volumes of MVPA (OR=0.79, 95% CI 0.65 to 0.97, model 2) compared to the group of individuals who engaged in less than 5 minutes per day of total MVPA. Similarly, participants in the highest tertile of LIPA had significantly lower odds of confirmed sarcopenia (OR=0.80, 95% CI 0.66 to 0.98, model 2) when compared to the lowest tertile of LIPA. However, after adjusting for chronic health conditions (model 3), the associations of MVPA and LIPA with confirmed sarcopenia were no longer significant. In comparison to individuals among the lowest tertile of SB (least sedentary

group), participants in the highest tertile of SB (most sedentary group) indicated 1.41 (95% CI 0.91 to 1.41) higher odds of confirmed sarcopenia in the fully adjusted model.

Severe sarcopenia: Individuals among the highest tertile of total activity counts had a significantly lower likelihood for severe sarcopenia (OR=0.85, 95% CI 0.73 to 0.99) in contrast to participants among the lowest tertile of total activity counts. Model 1 and model 3, however, demonstrated non-significant results of this association. The odds for severe sarcopenia were significantly lower among participants who spent 10 minutes or more per day in total MVPA (OR=0.85, 95% CI 0.73 to 0.99, model 2) compared to individuals with less than 5 minutes per day of total MVPA. Participants in the highest tertile of LIPA also demonstrated a significant association with severe sarcopenia (OR=0.85, 95% CI 0.73 to 0.99, model 2) when compared with participants among the lowest tertile of LIPA. The adjustment for comorbid conditions (model 3), however, attenuated the significance regarding the associations of MVPA and LIPA with severe sarcopenia. No significant associations were observed across tertiles of SB with severe sarcopenia.

Table 22: Dose-response associations of physical behavior volume metrics with sarcopenia status

Dose-response associations of TAC tertiles with sarcopenia status

	Total TAC (mean/SD)		
	First Tertile	Second Tertile	Third Tertile
n	29	29	29
TAC, mean (SD)	145,877 (44,216)	226,888 (21,107)	364,295 (94,771)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.01 (0.79 to 1.29)	0.85 (0.66 to 1.09)
Model 2	Ref	0.98 (0.77 to 1.25)	0.83 (0.65 to 1.06)
Model 3	Ref	0.98 (0.77 to 1.26)	0.84 (0.66 to 1.08)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	0.99 (0.80 to 1.23)	0.83 (0.67 to 1.03)
Model 2	Ref	0.95 (0.77 to 1.16)	**0.81 (0.66 to 0.99)**
Model 3	Ref	0.95 (0.78 to 1.16)	0.82 (0.67 to 1.00)
Severe sarcopenia (yes/no)			
Model 1	Ref	0.88 (0.76 to 1.03)	0.86 (0.74 to 1.00)
Model 2	Ref	0.86 (0.74 to 1.01)	**0.85 (0.73 to 0.99)**
Model 3	Ref	0.86 (0.74 to 1.01)	0.87 (0.74 to 1.01)

Dose-response associations of total MVPA groups with sarcopenia status

	Total MVPA (min/day)		
	0-5 min Group	5-10 min Group	≥10 min Group
n	45	18	24
MVPA, mean (SD)	2.8 (1.0)	7.0 (1.5)	22.5 (12.3)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.89 (0.69 to 1.16)	**0.74 (0.59 to 0.94**
Model 2	Ref	0.90 (0.69 to 1.16)	**0.77 (0.61 to 0.98)**
Model 3	Ref	0.89 (0.68 to 1.15)	0.79 (0.62 to 1.01)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	0.98 (0.78 to 1.22)	**0.75 (0.61 to 0.92)**
Model 2	Ref	0.98 (0.79 to 1.21)	**0.79 (0.65 to 0.97)**
Model 3	Ref	0.96 (0.77 to 1.19)	0.82 (0.67 to 1.00)
Severe sarcopenia (yes/no)			
Model 1	Ref	0.88 (0.75 to 1.03)	**0.83 (0.72 to 0.97)**
Model 2	Ref	0.88 (0.74 to 1.03)	**0.85 (0.73 to 0.99)**
Model 3	Ref	0.87 (0.74 to 1.03)	0.88 (0.75 to 1.02)

Dose-response associations of total LIPA tertiles with sarcopenia status

	Total LIPA (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	29	29	29
LIPA, mean (SD)	92.3 (30.2)	147.6 (11.7)	205.3 (35.7)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.91 (0.71 to 1.16)	0.88 (0.69 to 1.12)
Model 2	Ref	0.90 (0.71 to 1.15)	0.90 (0.71 to 1.15)
Model 3	Ref	0.92 (0.72 to 1.18)	0.92 (0.72 to 1.19)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	0.94 (0.76 to 1.15)	**0.78 (0.63 to 0.95)**

Model 2	Ref	0.93 (0.76 to 1.13)	**0.80 (0.66 to 0.98)**
Model 3	Ref	0.96 (0.78 to 1.17)	0.82 (0.67 to 1.00)
Severe sarcopenia (yes/no)			
Model 1	Ref	0.93 (0.80 to 1.08)	**0.84 (0.72 to 0.97)**
Model 2	Ref	0.92 (0.79 to 1.08)	**0.85 (0.73 to 0.99)**
Model 3	Ref	0.94 (0.80 to 1.09)	0.87 (0.75 to 1.01)

Dose-response associations of total SB tertiles with sarcopenia status

	Total SB (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	29	29	29
SB, mean (SD)	567.5 (46.0)	651.3 (26.8)	834.2 (135.3)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.99 (0.76 to 1.29)	1.20 (0.86 to 1.67)
Model 2	Ref	0.96 (0.73 to 1.25)	1.17 (0.83 to 1.64)
Model 3	Ref	0.91 (0.69 to 1.20)	1.14 (0.80 to 1.61)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	1.13 (0.91 to 1.42)	**1.47 (1.10 to 1.95)**
Model 2	Ref	1.09 (0.88 to 1.35)	**1.43 (1.09 to 1.88)**
Model 3	Ref	1.06 (0.85 to 1.33)	**1.41 (1.06 to 1.86)**
Severe sarcopenia (yes/no)			
Model 1	Ref	1.15 (0.98 to 1.36)	1.19 (0.97 to 1.47)
Model 2	Ref	1.13 (0.96 to 1.34)	1.18 (0.96 to 1.46)
Model 3	Ref	1.09 (0.92 to 1.30)	1.13 (0.91 to 1.41)

Notes: Bold values are significant. Probable or confirmed sarcopenia will be defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women), low muscle mass tested by a dual-energy X-ray absorptiometry (appendicular skeletal muscle mass: <20 kg for men and <15 kg for women), and low physical performance assessed by a 20-m usual walking speed test (gait speed: ≤0.8 m/s).
Abbreviations: LIPA: light intensity physical activity; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval); Ref: Reference; SB: sedentary behavior; TAC: Total activity counts.
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

Patterns: Table 23 demonstrates the dose-response associations of physical behavior pattern metrics with sarcopenic status classified by EWGSOP2, including probable sarcopenia, confirmed sarcopenia, and severe sarcopenia, in the subsample.

Probable sarcopenia: The group of participants with any time spent in long MVPA bouts (≥10 minutes) had 35% (95% CI 0.47 to 0.89) lower odds for a probable sarcopenia diagnosis compared to individuals who engaged zero time in long MVPA

bouts (≥10 minutes) after final adjustment. No significant associations were detected across tertiles of short MVPA bouts (<10 minutes), sedentary breaks, and ASTP with probable sarcopenia.

Confirmed sarcopenia: The likelihood for a confirmed sarcopenia diagnosis was 19% (95% CI 0.66 to 0.99, model 2) lower among participants in the highest tertile of short MVPA bouts (<10 minutes) compared to individuals in the lowest tertile of short MVPA bouts (<10 minutes). However, significant outcomes of this association were lacking in model 1 and model 3. There were also significant associations across tertiles of ASTP with confirmed sarcopenia in model 1 (second tertile: OR=1.24 95% CI 1.01 to 1.52; third tertile: OR: 1.27 95% CI 1.03 to 1.57), but further adjustments for lifestyle factors (model 2) and chronic health conditions (model 3) attenuated the associations. There were no significant associations across tertiles of long MVPA bouts (≥10 minutes) and sedentary breaks with confirmed sarcopenia.

Severe sarcopenia: Participants among the highest tertile of short MVPA bouts (<10 minutes) had 18% (95% CI 0.71 to 0.96) lower odds of severe sarcopenia compared to participants in the lowest tertile of short MVPA bouts (<10 minutes) after full adjustment. Furthermore, individuals in the highest tertile of ASTP demonstrated a 1.23 (95% 1.06 to 1.44, model 2) times higher likelihood for severe sarcopenia compared to participants in the lowest tertile of ASTP. The significance of this relationship, however, disappeared after the adjustment for chronic health conditions (model 3). There were no significant associations across tertiles of long MVPA bouts (≥10 minutes) and sedentary breaks with severe sarcopenia.

Table 23: Dose-response associations of patterns of physical behavior metrics with sarcopenia status

Dose-response associations of short MVPA bouts (<10 minutes) duration tertiles with sarcopenia status

	MVPA <10 minute bout (min/day)		
	First Tertile	Second Tertile	Third Tertile
n	30	28	29
MVPA <10 minute bout, mean (SD)	2.3 (0.7)	5.0 (1.3)	16.9 (10.2)
Probable sarcopenia (yes/no)			
Model 1	Ref	0.91 (0.71 to 1.17)	0.80 (0.62 to 1.03)
Model 2	Ref	0.89 (0.69 to 1.14)	0.80 (0.62 to 1.02)
Model 3	Ref	0.90 (0.70 to 1.16)	0.81 (0.63 to 1.05)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	1.01 (0.81 to 1.25)	0.81 (0.65 to 1.00)
Model 2	Ref	0.97 (0.79 to 1.19)	**0.81 (0.66 to 0.99)**
Model 3	Ref	0.98 (0.80 to 1.21)	0.82 (0.67 to 1.01)
Severe sarcopenia (yes/no)			
Model 1	Ref	0.92 (0.79 to 1.07)	**0.81 (0.69 to 0.95)**
Model 2	Ref	0.90 (0.77 to 1.05)	**0.81 (0.69 to 0.94)**
Model 3	Ref	0.92 (0.79 to 1.08)	**0.82 (0.71 to 0.96)**

Dose-response associations of long MVPA bouts (≥10 minutes) duration groups with sarcopenia status

	MVPA ≥10 minute bout (min/day)	
	No ≥10 minute bouts	≥10 minute bouts
n	76	11
MVPA ≥10 minute bout, mean (SD)	0.0 (0.0)	8.8 (6.7)
Probable sarcopenia (yes/no)		
Model 1	Ref	**0.63 (0.47 to 0.85)**
Model 2	Ref	**0.65 (0.49 to 0.87)**
Model 3	Ref	**0.65 (0.47 to 0.89)**
Confirmed sarcopenia (yes/no)		
Model 1	Ref	0.77 (0.59 to 1.00)
Model 2	Ref	0.81 (0.63 to 1.04)
Model 3	Ref	0.87 (0.67 to 1.14)
Severe sarcopenia (yes/no)		
Model 1	Ref	0.90 (0.74 to 1.09)
Model 2	Ref	0.02 (0.76 to 1.11)
Model 3	Ref	0.93 (0.76 to 1.14)

Dose-response associations of number of sedentary breaks tertiles with sarcopenia status

	Number of sedentary breaks (no. of breaks/day)		
	First Tertile	Second Tertile	Third Tertile
n	29	29	29
Sedentary breaks, mean (SD)	51.8 (12.7)	71.6 (3.5)	87.8 (6.6)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.04 (0.81 to 1.33)	0.90 (0.70 to 1.15)
Model 2	Ref	1.04 (0.81 to 1.34)	0.92 (0.72 to 1.18)
Model 3	Ref	1.06 (0.82 to 1.36)	0.94 (0.72 to 1.23)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	1.03 (0.83 to 1.27)	0.81 (0.65 to 1.00)

Model 2	Ref	1.03 (0.84 to 1.26)	0.82 (0.67 to 1.01)
Model 3	Ref	1.06 (0.87 to 1.29)	0.82 (0.67 to 1.02)
Severe sarcopenia (yes/no)			
Model 1	Ref	0.96 (0.82 to 1.13)	0.90 (0.77 to 1.05)
Model 2	Ref	0.96 (0.82 to 1.13)	0.91 (0.77 to 1.07)
Model 3	Ref	0.97 (0.83 to 1.14)	0.94 (0.79 to 1.11)

Dose-response associations of ASTP tertiles with sarcopenia status

	ASTP		
	First Tertile	Second Tertile	Third Tertile
n	29	29	29
ASTP, mean (SD)	0.37 (0.05)	0.48 (0.03)	0.61 (0.08)
Probable sarcopenia (yes/no)			
Model 1	Ref	1.23 (0.97 to 1.57)	1.16 (0.91 to 1.48)
Model 2	Ref	1.21 (0.95 to 1.54)	1.12 (0.88 to 1.43)
Model 3	Ref	1.19 (0.93 to 1.53)	1.04 (0.79 to 1.37)
Confirmed sarcopenia (yes/no)			
Model 1	Ref	**1.24 (1.01 to 1.52)**	**1.27 (1.03 to 1.57)**
Model 2	Ref	1.20 (0.98 to 1.46)	1.20 (0.98 to 1.48)
Model 3	Ref	1.17 (0.96 to 1.44)	1.11 (0.89 to 1.39)
Severe sarcopenia (yes/no)			
Model 1	Ref	1.08 (0.93 to 1.25)	**1.26 (1.08 to 1.26)**
Model 2	Ref	1.07 (0.92 to 1.24)	**1.23 (1.06 to 1.44)**
Model 3	Ref	1.06 (0.91 to 1.23)	1.18 (1.00 to 1.40)

Notes: Bold values are significant. Probable or confirmed sarcopenia will be defined using low upper limb muscle strength evaluated by a calibrated handgrip dynamometer (grip strength: <27 kg for men and <16 kg for women), low muscle mass tested by a dual-energy X-ray absorptiometry (appendicular skeletal muscle mass: <20 kg for men and <15 kg for women), and low physical performance assessed by a 20-m usual walking speed test (gait speed: ≤0.8 m/s). The active-to-sedentary transition probability index is calculated by dividing the total number of breaks in sedentary behavior with the sum of minutes spent in physical activity.
Abbreviations: ASTP: active-to-sedentary transition probability; MVPA: moderate to vigorous physical activity; OR (95% CI): odds ratio (95% confidence interval).
Model 1: adjusted for age, gender, race, education, accelerometer wear time
Model 2: model 1 + lifestyle factors (BMI, smoking status)
Model 3: model 2 + chronic health conditions (diabetes, hypertension, history of cardiovascular disease, history of cancer)

CHAPTER 5

DISCUSSION

The aim of this study was to gain a better understanding regarding the associations of various accelerometer-determined physical behavior metrics with sarcopenia status and its components among oldest-old adults. Cross-sectional data from the Health ABC cohort study of community-dwelling oldest-old adults with a mean age of 88.2 (2.5) years helps address our research aims. As described in Chapter 3, we created two different samples for this secondary analysis. The primary sample with a total of 145 participants focused on the associations of physical behavior metrics with EWGSOP2 defined probable sarcopenia and handgrip strength. Moreover, the subsample with 87 participants looked at the associations of physical behavior metrics with EWGSOP2 defined probable, confirmed, and severe sarcopenia as well as their related components including handgrip strength, appendicular lean mass, and gait speed. The findings of this study correspond with our hypotheses by highlighting that higher volumes of MVPA, regardless of its accumulation in short MVPA bouts (<10 minutes) or long MVPA bouts (≥10 minutes), are associated with lower odds of EWGSOP2 defined sarcopenia and better sarcopenia-relevant indicators among oldest-old adults.

5.1 Associations of Physical Behavior Volume Metrics with Sarcopenia

The first main subject of discussion represents the interpretation of our study findings regarding the associations of physical behavior volume metrics, including total activity counts, total MVPA, total LIPA, and total SB, with sarcopenia and its components in due consideration of previous research.

First, there were no significant associations of total activity counts with probable, confirmed, or severe sarcopenia in our study. These results are not in line with prior examinations which demonstrated that objectively measured total activity counts are related with sarcopenia and its components.[64,90] Westbury et al.[90] and Sanchez-Sanchez et al.[64] observed that higher total activity counts were associated with lower odds of EWGSOP defined sarcopenia and FNIH defined sarcopenia, respectively. The variety of used sarcopenic definitions among previous analyses hinders the comparability of provided study outcomes.[20,21] In this context, dissimilarities exist between the original EWGSOP definition and the revised EWGSOP2 definition in terms of their different cut-off values.[22] For instance, while EWGSOP identifies low handgrip strength as <30 kg for men and <20 kg for women, the EWGSOP2 algorithm diagnoses low handgrip strength with cut-off points of <27 kg for men and <16 kg for women which leads to considerable dissimilarities regarding the sarcopenia prevalence rates.[131]

Furthermore, our study outcomes indicate that accelerometer-determined MVPA was significantly associated with a lower likelihood of sarcopenia which is in agreement with previous research.[64,66] In this regard, each 5 minutes more per day of MVPA was related with 27% lower odds for a probable sarcopenic condition among oldest-old adults. Despite non-significant associations of total MVPA volumes with sarcopenic conditions in the subsample, we observed a trend that each 5 minutes more per day in MVPA was related with lower odds of probable and confirmed sarcopenia. The attenuated significance in the subsample might be caused by the reduced sample size and the related loss of statistical power. Non-significant findings regarding the associations of accelerometer-assessed MVPA with sarcopenia are not uncommon. For instance, studies

from Aggio et al.[96] and Westbury et al.[90] were also not able to identify any significant association between objectively measured MVPA and EWGSOP defined sarcopenia. Likewise, results of the dose-response analysis indicated that the daily volume of MVPA should exceed 10 minutes in order to significantly lower the odds of probable sarcopenia. These findings suggest that engaging more time in MVPA may be associated with lower odds of sarcopenia among oldest-old adults.

A non-significant relationship between LIPA and probable sarcopenia was illustrated among our primary sample. However, after applying the full EWGSOP2 algorithm to determine the diagnostic state of sarcopenia,[18] there were associations with the likelihood of confirmed and severe sarcopenia. Participants who engaged more time in LIPA had 18% and 13% lower odds of confirmed and severe sarcopenia, respectively. In this context, a recent randomized controlled trial study with 28 older women reported that 8 weeks of SB displacement with LIPA (45-50 minutes daily) significantly improved handgrip strength and gait speed.[132] This is a promising finding since LIPA can be better sustained than MVPA by older adults.[132] Consequently, LIPA might be an encouraging concept for future health guidelines to improve or maintain musculoskeletal health among oldest-old adults.

Several studies have reported that accelerometer-determined SB levels are not related with the prevalence of sarcopenia among older adults.[66,96,115] In our sample of oldest-old adults, spending 60 minutes more per day in SB was associated with a 2.10- and 3.79-times higher likelihood for confirmed sarcopenia and severe sarcopenia. More research is needed to clarify the influence of SB on musculoskeletal health in oldest-old

adults which might contribute crucial information for future health guidelines.[111] Overall, high levels of SB may be associated with lower odds of confirmed and severe sarcopenia.

With the focus on sarcopenic components, our study outcomes are in agreement with previous research, showing that higher total activity counts,[64,90] higher MVPA,[64,96] and higher LIPA[96] were associated with better gait speed. On the other hand, higher SB was associated with worse gait speed which is also in line with prior studies.[91,96] Modifications of physical behavior volume metrics by spending more time in active and less time in sedentary behavior might help enhance the physical performance of oldest-old adults. These performance improvements may provide a vital contribution for better muscle health which is a key factor for independence and thus a higher quality of life among the oldest-old adult population.[133,134]

5.2 Associations of Physical Behavior Pattern Metrics with Sarcopenia

The second main subject of discussion represents the interpretation of our study findings regarding the associations of physical behavior pattern metrics, including short MVPA bout duration (<10 minutes), long MVPA bout duration (≥10 minutes), total number of sedentary breaks, and ASTP, with sarcopenia and its components in due consideration of prior examinations.

Recent studies have shown that the accumulation of MVPA levels with short bouts of less than 10 minutes contribute to the improvement of various health-related outcomes.[62,63] To the best of our knowledge, this is the first study to look at the association of accelerometer-determined short MVPA bouts with sarcopenia status and its components. Interestingly, our study outcomes indicated that higher accumulated time spent in short MVPA bouts was associated with lower odds of any sarcopenic condition,

including probable, confirmed, and severe sarcopenia. In this context, Hrubeniuk et al.[135] reported that each minute spent in MVPA led to significantly better physical function among older adults. These findings underscore the potentially positive impact of short MVPA bouts on sarcopenic status among oldest-old adults. Encouraging oldest-old adults to accumulate high levels of MVPA without the need to sustain bouts lasting longer than 10 minutes might be beneficially associated with muscle-related health.

Study results from Scott et al.[66] indicated that the accumulated time spent in MVPA bouts longer than 10 minutes was significantly associated with a lower likelihood of probable or confirmed sarcopenia.[66] This is congruent with the outcomes provided in our primary sample since each 5 minutes more time engaged in long MVPA bouts indicated 69% lower odds for a probable sarcopenic state. Findings of the dose-response analysis exhibited that participants who spent at least some time in long MVPA bouts had a lower likelihood for a probable sarcopenic condition compared to individuals who engaged zero minutes in long MVPA bouts. However, only a small fraction of people at this age might be able to engage in long MVPA bouts. Just 21(14.5%) participants in the primary sample and a total of 11 (12.6%) participants in the subsample provided at least some minutes in MVPA bouts lasting longer than 10 minutes. A low frequency of long MVPA bouts was expected due to the advanced age of included individuals. Unfortunately, the absence of a normal distribution and the high number of participants with zero minutes spent in long MVPA bouts resulted in a limited ability to statistically compute binomial logistic regressions in the subsample. This also restricts our capability to directly compare shorter vs. longer bouts of MVPA in this sample, since so few individuals accumulated MVPA in longer bouts. Recent evidence reported that older

adults prefer to participate in short MVPA bouts compared to long MVPA bouts which might indicate an increased tolerance to accumulate high levels of MVPA minutes via short sporadic bouts.[135] In addition, Menai et al. (2017) reported that higher time spent in short MVPA bouts was similarly associated with successful aging (defined as a combination of better cognitive, motor, and respiratory functions as well as absence of major chronic diseases) as when MVPA was accumulated in prolonged bouts among older adults. Consequently, short MVPA bouts might be a feasible and efficient alternative to maintain or improve muscle health among oldest-old adults.

We did not find any significant association of sedentary breaks with probable, confirmed, or severe sarcopenia. Prior investigations have also indicated no relationship between the total number of objectively measured sedentary breaks and sarcopenia.[96,115] Interestingly, higher numbers of daily sedentary breaks were associated with higher appendicular lean mass which is not in accordance with the results from Aggio et al.[96] who found no association. Frequent interruptions of SB might lead to a multitude of additional contractions throughout the day which in turn may cause alterations in the muscle expression of genes responsible for cellular development, growth and proliferation, and carbohydrate metabolism.[136,137] This physiological process might benefit the musculoskeletal health among older adults. However, epidemiological research has provided inconclusive evidence with respect to the relationship between sedentary breaks and muscle mass.[111]

The analysis of the activity fragmentation in older adults via the active-to-sedentary transition probability (ASTP) index is a promising concept for quantifying patterns of activity, particularly in aging populations.[48] As we age, we might expect a

dramatic change of activity profiles due to functional declines.[48] In this context, PA patterns frequently become more fragmented among older adults due to emerging difficulties in sustaining PA bouts for a longer period of time.[50] Fragmented daily PA patterns, characterized by a higher ASTP index, have been linked with various detrimental health outcomes including poor physical performance,[48] greater fatigability,[50] cognitive impairment,[51] and a higher mortality risk in the older adult population.[49] This is the first study we are aware of to identify the association of accelerometer-determined ASTP with sarcopenia status and its components. Outcomes of the subsample demonstrated that each 0.1 higher ASTP was linked with 2.90 times greater odds for a severe sarcopenia diagnosis. Focusing on individual components of sarcopenia, higher ASTP showed an association with lower gait speed in both genders. Similar findings were reported by Schrack et al.[48], where higher ASTP was also related with worse gait speed performance among older adults. Therefore, oldest-old adults with less fragmented activity patterns might demonstrate associations with a lower likelihood of severe sarcopenia and better gait speed. Comparable outcomes were provided by Chastin et al.[138], who showed a significant relationship between less fragmented activity patterns and better muscle quality among older adults. In this context, the ASTP index might be a useful marker for the assessment of accelerated biological aging[51] and thus a predictor for the onset and/or severity of sarcopenia. ASTP does not address differences in total volume of PA. For instance, an individual who obtains 100 minutes of activity with 10 breaks would provide the same ASTP score as an individual who obtains 10 minutes of activity with 1 break (ASTP = 0.1 for both). Therefore, ASTP may better represent physical function than levels of PA. Activity fragmentation in which older adults need to

break up activity more often might be an early sign for poorer physical function. Furthermore, we should note that the utilization of activity fragmentation calculations may be most applicable in old adult populations rather than young adult populations due to the presence of functional declines with advancing age.[48] Consequently, accelerometer determined activity fragmentation metrics such as the ASTP index might serve as a valuable indicator of functional declines among older adults.

5.3 Strengths and Limitations

This study benefits from a comprehensive data set among a sample of the oldest-old adult population which includes measures of demographic and lifestyle factors, chronic health conditions, muscle strength, muscle mass, physical performance, and accelerometry. Owing to the availability of ActiGraph GT3X+ accelerometer data, we were able to analyze the association of various physical behavior metrics with EWGSOP2 defined sarcopenia and its determinants. This approach allowed us the investigation of relationships with clinically relevant sarcopenia definitions as well as the underlying factors of handgrip strength, appendicular lean mass, and gait speed. Tri-axial accelerometry is considered a relatively valid and reliable method of evaluating free-living behavior which provides a detailed estimation of activities in terms of their volume and intensity.[58] Accelerometer data are provided by a demographically diverse community-dwelling population with a high mean age of 88.2 (2.5) years. Another strength of our study is the employment of the EWGSOP2 sarcopenia definition which is widely accepted and endorsed by a range of international scientific societies.[18] Moreover, we utilized DXA-scan data in order to assess muscle mass in our sample. DXA provides more accurate and reliable estimations of muscle mass compared to other evaluation

methods such as anthropometric measures or BIA.[18] We also created 3 different models with the purpose to adjust for several key covariates including various demographic factors plus accelerometer wear time (model 1), lifestyle factors (model 2), and chronic health conditions (model 3). All these covariates have shown connections with sarcopenic conditions and their components. In addition, this study provided novel insights into the associations of short MVPA bouts (<10 minutes) and ASTP with EWGSOP2 defined sarcopenia and its components.

Our analysis has several limitations. Due to the cross-sectional study design, we cannot infer causalities regarding the associations of physical behavior metrics with sarcopenic conditions and their determinants. Despite our hypothesis that higher levels of intense PA levels are associated with lower sarcopenia-relevant indicators, there is also the possibility of a reverse causality in which diminished muscle strength, muscle mass, or physical performance induce lower volumes and intensities of PA. In addition, we had to remove all Pittsburgh-dwelling individuals from our subsample because of the unavailability of DXA-scan data. Removing those participants considerably reduced the statistical power of our subsample analysis. Furthermore, there was a low number of oldest-old adults with long MVPA bouts which limited our ability to investigate associations of long MVPA bouts with sarcopenia and its components. Although we adjusted for a variety of covariates, there remains a possibility of residual confounding. For example, potential covariates such as malnutrition or osteoporosis were not collected at year 16 and therefore not included in our study. Unfortunately, despite being the most rapidly increasing population,[7] specified accelerometer cut-off points to determine PA intensities among oldest-old adults are not available in the current literature. The absence

of an accelerometer-specific standardized protocol for the oldest-old adult population is considered a substantial limitation since physical function decreases at an annual rate of approximately 4% after the age of 65 years.[139] Due to age-related physical declines and related alterations of walking patterns, an oldest-old adult at the age of 85 years might show a higher energy expenditure for the same activity compared to an older adult at the age of 65 years.[140] Consequently, a lower cut-point for MVPA than that provided by Copeland et al.[130] may be appropriate for oldest-old adults in order to obtain more accurate evaluations of their physical behavior metrics. We should also note that the limited ability of ActiGraphs to distinguish between LIPA and SB might lead to a misclassification of behavioral activities.[141,142] In this context, standing activities such as washing dishes or folding laundry are often disregarded by accelerometers.[141,142] Hip-worn ActiGraphs also present difficulties in capturing data of upper body movements which have demonstrated strong associations with sarcopenia and its components.[35,142,143] Furthermore, because participants were instructed to remove the accelerometers during water-related activities, data of muscle-health-promoting aquatic exercises were also disregarded in our study.[144] Nevertheless, missing information about these activities may not pose a major limitation for our analysis since previous research has shown that the vast majority of older adults prefer to spend most of their active time in ambulatory activities such as walking which can be estimated with a relatively high accuracy by hip-worn accelerometers.[142,145,146]

CHAPTER 6

CONCLUSION

Modifiable characteristics of physical behavior offer promising opportunities to maintain or improve the musculoskeletal health in oldest-old adults. Our study findings contribute valuable knowledge to geriatric research by identifying cross-sectional associations of accelerometer-determined various physical behavior metrics with EWGSOP2 defined sarcopenia and its components among the oldest-old adult population. Higher volumes of MVPA, regardless of its pattern of accumulation, demonstrated associations with lower odds of probable sarcopenia in our primary sample. Consequently, accruing MVPA in long bouts might not be necessary to lower the likelihood of a probable sarcopenia diagnosis. This is an important finding for an increasingly aging population which seems to have difficulties sustaining prolonged MVPA bouts of at least 10 minutes.

Following the application of the full EWGSOP2 definition in the subsample, higher volumes of LIPA demonstrated associations with a lower likelihood of confirmed and severe sarcopenia. Additionally, greater odds of confirmed and severe sarcopenia were related with higher volumes of SB. This study also observed novel evidence that higher fragmented activity patterns were associated with severe sarcopenia and lower gait speed, indicating that activity fragmentation assessments might serve as a valuable index to detect severely deteriorated musculoskeletal health among the oldest-old adult population. The results of the dose-response analyses illustrated that most physical behavior metrics show significant associations with sarcopenic status in the highest tertile or group, while almost no significant links were seen among the second tertile or group.

This may provide the opportunity to define specific doses of daily physical behavior which might help lower the odds of sarcopenia in the oldest-old adult population. With focus on individual components of EWGSOP2 defined sarcopenia, our findings suggest that especially higher levels of PA, including total activity counts, MVPA, and LIPA, were associated with better gait speed. Therefore, physical function among oldest-old adults might be better preserved when overall greater volumes of PA are realized.

Based on the findings of our study, we can conclude that patterns of accumulated MVPA had an equally strong association with sarcopenia as the total volume of MVPA, highlighting the fact that short sporadic MVPA bouts might help maintain or improve musculoskeletal health in oldest-old adults. Overall, short MVPA bouts should gain more attention in geriatric research since they may provide information that can help design feasible and muscle-health promoting PA recommendations for the oldest-old adult population.

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